The Global Micronutrient Goals: lessons learned, analysis and the way forward (1990-2005)

Ian Darnton-Hill

A thesis submitted in fulfillment of the degree of Doctor of Philosophy

School of Human Life Sciences
University of Tasmania, Launceston
Australia

March 2008

The Global Micronutrient Goals: lessons learned, analysis and the way forward (1990-2005)

By

Ian Darnton-Hill,MBBS, MPH, MSc(Med), DipNutrDiet, FAFPHM, FACN

A thesis submitted in fulfillment of the degree of Doctor of Philosophy

School of Human Life Sciences
University of Tasmania, Launceston
Australia

March 2008

TABLE OF CONTENTS

LIST of TABLES

LIST of FIGURES

Contents of CD-Rom

1. List of published articles related to the thesis topic

2. pdfs of the articles

3. Participation in international expert groups and technical meetings related to micronutrients

4. Current curriculum vitae

DECLARATION

I certify that this thesis contains no material which has been accepted for the award of any other degree or diploma in any Institute, College or University, and that, to the best of my knowledge and belief, it contains no material previously published or written by another person except where due reference is made in the text.

Ian Darnton-Hill

STATEMENT OF AUTHORITY OF ACCESS

This thesis may be made available for loan and limited copying in accordance with the *Copyright Act 1968.*

Ian Darnton-Hill

ACKNOWLEDGEMENTS

In the preparation of this analytical review of the last decade and a half of global progress in the prevention and control of vitamin and mineral deficiencies, or micronutrient malnutrition, I have been grateful for the flexibility shown by the University

In the preparation of this analytical review of the last decade and a half of global progress in the prevention and control of vitamin and mineral deficiencies, or micronutrient malnutrition, I have been grateful for the flexibility shown by the University of Tasmania to allow me to complete it while working in full-time positions. Most recently UNICEF has been especially helpful, both with Library facilities and also granting me a week's study leave to help complete the task that had already gone on far too long.

I would like to particularly thank my supervisers, Professor Madeleine Ball and Dr Iain Robertson of the Launceston Campus of the University of Tasmania. They have gone out of their way to be helpful, including giving me accommodation on two occasions in their house when I was visiting the University from my overseas postings. Madeleine has been a source of strength and encouragement, not least when I was losing energy as I dealt with two jobs (acting in a position for three years) and the thesis was dragging-on. I am also grateful for her flexibility and especially for the wise advice to limit the scope to 1990 to 2005.

Another critical source of help and support has been Associate Professor Dominic Geraghty, Deputy Head of the School and who has been extremely helpful in the mechanics of submitting a thesis from off the campus and always cheerful in his help. I am very grateful also to Ms Merran Rogers who really helped to pull the formatting together at a long distance.

Others who have been helpful along the way are Ms. Beth Kopecky, my Administrative Assistant and friend at UNICEF, Ms Tiya Habachy, Mr Eunchul Bae and Ms Claire Cullen who helped with various formatting issues and getting the CD-Roms in order. Finally I would like to thank my daughter Phoebe Hill who is just embarking on the same, but hopefully shorter process, and her mother Dr Johanna Watson, always supportive. I would also like to thank friends and colleagues in UNICEF, WHO and WFP, amongst other partners, who shared their experiences, strategies and unpublished documentation, and many supportive friends, including Ken Kim.

Glossary

ACC/SCN	U.N. Administrative Coordinating Committee/Subcommittee on Nutrition
ARVs	Antiretroviral pharmaceuticals
CDC	Centers for Disease Control and Prevention (USA)
CEE/CIS	Central and Eastern Europe, Commonwealth of Independent States and Baltic States (UNICEF Region)
CHERG	Child Health Epidemiological Research Group
CIDA	Canadian International Development Agency
CGIAR Research	Consultative Group on International Agricultural
DARs	Damage Assessment Reports
DHS	Demographic and Health Surveys (USAID)
EAP	East Asia and Pacific Region (UNICEF Region)
EPI	Expanded Programme on Immunization
FAO Nations	Food and Agricultural Organization of the United
FFI	Food Fortification Initiative
FIVIMS	Food Insecurity & Vulnerability Information Mapping Systems
GAIN	Global Alliance for Improved Nutrition
Hb	Haemoglobin
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immunity Disease Syndrome
HKI	Helen Keller International
ICCIDD	International Council for Control of Iodine Deficiency Disorders
IAGSM	Inter-Agency Group for Safe Motherhood
IDA	Iron deficiency anaemia
ID	Iron deficiency most usually but has also been used for iodine deficiency
IDD	Iodine deficiency, iodine deficiency disorders
IDPAS	Iron deficiency project advisory service
IDRC (Canada)	International Development Research Council
IFPRI	International Food Policy Research Institute (part of CGIAR)
INACG	International Nutritional Anemia Consultative Group
INF	International Nutrition Foundation (based in Tufts University)
INGO	International Non-Governmental Organization

IOM	Institute of Medicine (of the National Academies, USA)
IVACG	International Vitamin A Consultative Group
IZiNCG	International Zinc Consultative Group
JHCP	UNICEF/WHO Joint Committee on Health Policy
MD	Millennium Declaration
MDG(s)	Millennium Declaration Goal(s)
MDIS	Micronutrient Deficiency Information System
MI	The Micronutrient Initiative
MICS	Multiple Indicator Cluster Survey (UNICEF)
MNM	Micronutrient Malnutrition
MOST	Micronutrients Operational Strategies & Technologies /USAID Micronutrients Program
MTCT	Mother to Child Transmission (of HIV)
NGO	Non-Governmental Organization
NIDs	National Immunization Days for the Eradication of Poliomyelitis
NMDs/NMWs	National Micronutrient Days/Weeks
NPAN	National Plan of Action for Nutrition
OMNI	Opportunities for Micronutrient Interventions
ODA	Overseas Development Aid
PAMM	Program Against Micronutrient Malnutrition (Emory University, Atlanta, Georgia)
PHC	Primary Health Care
PMNCH	Partnership for Maternal, Neonatal and Child Health
PRSP	Poverty Reduction Strategy Papers
PVO	Private Voluntary Organization
ROSA	South Asia (UNICEF Region)
SCN	Standing Committee on Nutrition of the U.N. System (previously ACC/SCN)
SES	Socio-economic Status
SOWC	State of the World's Children
SSA	Sub-Saharan Africa
SWAps	Sector Wide Approaches to national financing
TAC	The Americas and Caribbean (UNICEF Region)
TGR	Total goitre rate
U5MR	Under-five (years) mortality rate
UN	United Nations
UNDP	United Nations Development Programme
UNGASS	U.N. General Assembly Special Session (on Children)
UNICEF	United Nations Children's Fund

UNU	United Nations University
USAID	The United States of America Agency for International Development
USI	Universal Salt Iodization
VA	Vitamin A
VAD, VADD	Vitamin A deficiency, vitamin A deficiency Disorders
VAS	Vitamin A supplementation
VMD	Vitamin and Mineral Deficiency/Deficiencies
WFFC	World Fit for Children (UN Goals)
WFP	World Food Program of the United Nations System
WHO	World Health Organization
WSC	World Summit for Children (UN Goals)

Abstract

Micronutrient malnutrition, deficiencies of vitamins and minerals, affects one in three children in the world today, more than 2 000 million people, resulting in an enormous public health impact on the numbers of premature deaths in women and children particularly. These deficiencies, and their interaction with other health and care modalities, cause widespread morbidity, reduced intellectual potential, and an overall negative impact on national development and economic growth. To address this, global goals were established for the elimination or significant reduction of the prevalence of these deficiencies. The three micronutrient deficiencies of current greatest public health significance are iron, vitamin A and iodine, although zinc is receiving increasing attention, as is folate, vitamin B12 and other micronutrients in emergency situations. The thesis emphasized vitamin A as an example, while recognizing that different approaches to prevention and control will also be needed to adequately address other micronutrients. One aim of the thesis was to identify constraints and facilitating factors contributing to the success, or otherwise, towards achieving the first set of international micronutrient goals by the stated date of the end of the previous decade (2000). The programmes and policy decisions used in addressing micronutrient malnutrition were described and critically examined. This analysis was then used to examine this current decade (2000-2010) and the new decade goals of the UN Special Session of the General Assembly on Children. Since then the Millennium Development Declaration and Goals have to a large extent become the overarching global framework of goals, with the earlier goals being the basis for work planning and implementation. The hypothesis that the first set of international micronutrient goals was not reached globally because identifiable steps and pre-conditions were not met was addressed through access to a variety of sources, including a literature review through Medline and the search machines used by the Library systems of UNICEF, Columbia University and the University of Tasmania, with follow-up of likely articles or documents found from these identified articles. These were supplemented by national and United Nations system reports (especially WHO and UNICEF but also UNDP, World Bank and WFP), and the author's current daily work activities contributed significantly to the final product. Based on this approach, identification of trends, commonalities, and differences, were part of the analysis, taking into account cultural, socio-economic, resources and epidemiological variety of the many countries involved. This analysis led to a suggested re-interpretation of why micronutrients have over the last decade and a half become so

prominent in international public health priorities; to a compilation and analysis of constraints and facilitating factors. There is no doubt there has been enormous progress, particularly over the last two decades. Both constraints and facilitating factors were summarized, using the UNICEF Nutrition framework under four broad areas: basic or global (mega-) factors; underlying or national (macro-) factors; underlying or sub national (meso-) factors; and, proximal or immediate community and household factors (micro-), and by matrices. In essence the main factors included: (i) demonstrated commitment by government and a relevant policy in place; (ii) a knowledge of the magnitude of the problem; (iii) an awareness of the public health and social consequences by all levels; (iv) an intersectoral approach; (v) an awareness of the direct link to poverty, socio-economic and politico-social issues, and hence the need to address these specifically, as part of micronutrient deficiencies prevention and control programmes; (vi) initial presence of external funding; and, (vii) a 'champion' both internationally and nationally. National and local factors also played different roles in different settings. Firstly, micronutrient interventions were often not integrated at the community and district level e.g. vitamin A capsules and immunization were very infrequently integrated, except for the relatively short-lived National Polio Immunization Days, including having separate reporting systems and being implemented by different sections of the Health Ministry. Secondly, the micronutrient programmes, including universal salt iodization (USI), were often seen as externally driven e.g. by donors, or in the case of USI as a 'UNICEF Programme'. As part of this, the goals were sometimes seen as an external, international goal, not necessarily as relevant to the perceived or documented needs of the country, despite virtually all countries having signed off on them. Thirdly, clearly ineffectual programmes continued to be promoted e.g. iron/folic acid supplementation. Fourthly, inadequate health and other systems with poor infrastructure and inadequate staffing have made delivery of many health interventions, including micronutrient supplementation, difficult. Finally, in the face of continuing and often increasing social disparities and other inequities, for most poor populations, diets are unlikely to improve sufficiently, and in the short run at least, neither will delivery systems.

Chapter One

1.1 Aims and outline

It has been estimated that micronutrient malnutrition affects one in three children in the world today. These deficiencies impact enormously on the numbers of premature deaths in women and children particularly and on their morbidity, as well as causing reduced intellectual potential and an overall negative impact on national development and economic growth. Micronutrient malnutrition has become a frequently used descriptor for deficiencies of public health significance of vitamins and minerals, and especially of vitamin A, iron and iodine. To address this global public health problem, global goals were established for the elimination or significant reduction of the prevalence of these conditions. These will be discussed in more detail in Chapters 4 and 7, but were:

(a) Reduction of iron deficiency anaemia in women by one third of the 1990 levels;
(b) Virtual elimination of iodine deficiency disorders; and
(c) Virtual elimination of vitamin A deficiency.

Aims

(1) The first aim of this thesis is to identify constraints and facilitating factors contributing to the success, or otherwise, towards achieving the first set of international micronutrient goals by the stated date of the end of the previous decade (2000) (UNICEF 1990a). The programmes and policy decisions used in addressing micronutrient malnutrition will be described and critically examined.

(2) The thesis also aims to use this analysis to examine this current decade and the new goals that have since been adopted. These were not in place at the initial time of writing but are now firmly in place following the UN Special Session of the General Assembly on Children in May 2002 which led to the adoption of new UN Goals, with UNICEF as the responsible body (UNICEF 2002a). Since then the Millennium Development Declaration and Goals have to a large extent become the overarching global goals (UN 2002a, UN 2002b, World Bank

2004a), with the various earlier goals being the basis for work planning and implementation (UNICEF 1990, FAO/WHO 1992, UNICEF 2002a, WHO 2003a).

The basic assumptions are that:

1. There are common sets of necessary factors that are common to successful programmes
2. Conversely, there are factors and situations that if not in-place, make success less likely

These will be identified, and discussed within the thesis but include:

- commitment by government and a relevant policy in place
- knowledge of the magnitude of the problem
- an awareness of the consequences
- an intersectoral approach
- a need to also address poverty, socio-economic and social issues
- initial presence of external funding
- a 'champion' both internationally and nationally

The **hypothesis** could therefore be stated as:
that the first set of international micronutrient goals was not reached globally because identifiable steps and pre-conditions were not met.

1.2 Method

Much of the available information had been accumulated by the author in the course of his work, from a variety of sources. A literature review was conducted using Medline and the search machines used by the Library systems of UNICEF, Columbia University and the University of Tasmania, with follow-up of likely articles or documents found from these identified articles e.g. where referenced, but not found in the searches. These were supplemented by national and United Nations system reports (especially WHO and UNICEF but also UNDP, World Bank and WFP) and other unpublished reports and proceedings that the author had access to, or was involved in the development of. Further consolidation and analysis of the literature made use of the extensive in-country and international involvement of the author, supported by his previously published work in the broad area of micronutrient malnutrition (as in the CD-Rom attached at end of this

thesis). The underlying concept of this work is that the author's current daily work activities contribute significantly to the final product. Based on this approach, identification of trends, commonalities and differences were part of the analysis, taking into account cultural, socio-economic, resources and epidemiological variety of the many countries involved.

Writing the thesis while working full-time clearly had advantages such as access to the most recent information, an active role in international policy development, and in national programme evaluation. Conversely the time constraints meant that the work has been spread over many years. There were two consequences, at least, of this: firstly, that separate chapters were written over time and tend to be somewhat stand-alone, as well as part of the whole; and secondly, a decision was made to limit the historical time-frame to 1990 to 2005. Nevertheless, there are some more recent references where particularly pertinent, and some more recent prevalence and programme coverage data are used in chapter five. A conscious decision was also made to reference the author's own published work whenever possible to demonstrate the long and active involvement that underpins this thesis.

To address the aim of the thesis in identifying facilitating and inhibiting factors, the author reviewed the many sources mentioned, and then sorted by pre-assigned headings and grouped them. These sorts were then reviewed and categories reduced and commonalities identified, which are then discussed, and extrapolations and conclusions made. This was done by reviewing standard published reviews for the scientific background to the micronutrients discussed. Trends were identified by tracking surveillance systems used by the World Health Organization and UNICEF and assisted by other tracking groups such as the University of Tulane, the Micronutrient Initiative, Helen Keller International and the USAID Population, Health and Nutrition Center (through the OMNI and MOST Projects). Other sources were drawn upon as available- both published, for example, a report of the 2002 IVACG meeting (Ramakrishnan & Darnton-Hill 2002) and unpublished reports that the author had access to through working with the World Health Organization and subsequently as UNICEF Senior Adviser, Micronutrients. The author was also previously Director of the OMNI Project (Opportunities for Micronutrient Interventions). When that was completed as scheduled (OMNI 1995), analysis of its successes, failures and next steps started the

process, in a very preliminary way, resulted in this overview and conclusions, almost ten years later. Based on these experiences, the approach made uses both observational methods and triangulation of others' data sets and conclusions for validation of the main findings and conclusions.

Consequently, apart from author involvement in a UNICEF study of 20 countries completed with the Micronutrient Initiative (Aguayo et al., in press), and in the helping to design the information needs with University of Tulane for trends data required by UNICEF, what is new in this analytical overview is: a re-interpretation of why micronutrients have over the last decade and a half became so prominent in international public health priorities- first preliminarily suggested in 1999 (Darnton-Hill 1999a); compilation and analysis of constraints and facilitating factors, both by revisiting the published literature, reviews of programmes and also by being part of the 20-country analysis of vitamin A programmes as mentioned above; and by extrapolating these factors (based on the University of Tulane analysis of largely UNICEF data (Helwig, Rivers, Mason 2004) to likely future success. The other aspect that makes this work unique is the cross-disciplinary combination of an historical perspective along with the technical and public health nutrition core of the thesis. The author is probably one of the few who, from a variety of organizational perspectives, is in a position to do this.

The following outline has been used:
An introduction to the background of micronutrient malnutrition:

- Vitamin A deficiency, epidemiology and consequences
- Iodine deficiency and the iodine deficiency disorders
- Iron deficiency anaemia and other nutritional anaemias
- Other micronutrients of public health significance

This will be followed by further background information on the methods of control and prevention of micronutrient malnutrition:

- Prevention, control and treatment
- Food-based approaches, including fortification
- Supplementation
- Other public health approaches.

This background is considered necessary to understand the differences in approaches and outcomes when addressing deficiencies of the three micronutrients. Throughout the thesis there will be an emphasis on vitamin A as the illustrative micronutrient (largely reflecting greater experience with this particular micronutrient), with contrasts and examples from the prevention and control of iron deficiency anaemia, iodine deficiency disorders and other micronutrient deficiencies, where these demonstrate a particular point. The international commitments and national responses made at the various international fora, the actual goals and subsequent mid-term goals will then be discussed. There will be a brief discussion of why micronutrient malnutrition achieved this relatively sudden consensus as an international public health priority.

Next, the results of this global attention will be reported from available literature and reports, and from these the progress that had been made by the end of the decade (December 31, 2000). More recent progress, or sometimes the lack of it, since the end of the decade (up to 2005, with projections beyond), will be also be described to show on-going trends. This progress, or lack of it in the case of iron deficiency anaemia, will be discussed in terms of lessons learned and what have been facilitating factors and inhibiting factors. A framework, according to level of social organization and governance, will be constructed showing identified constraints and facilitating factors. Finally, conclusions and predictions will be made on this, more than halfway through the next decade, looking at the new goals and their rationale and feasibility.

As already noted, the above will be supported by a review of the published literature, including the use of UN Agency reports, and unpublished planning documents, reports and evaluations. Articles, chapters and guidelines published by the author will provide the background to many of the chapters and will link the body of work to combine theory and practical experience. Although enclosed separately, they represent an integral part of the thesis.

The author was at the time of much of the early writing a Senior Global Health Leadership Fellow at the World Health Organization. Immediately prior to that he had the responsibility for overseas programmes in an international non-governmental organization (INGO), Helen Keller International (HKI), which has been in existence for 85 years, primarily for the prevention and rehabilitation of blinding diseases. In the mid-

1980s, the aetiology of one of its traditional areas of interest/involvement, xerophthalmia (or 'nutritional blindness') caused by vitamin A deficiency, was also found to have a profound effect on premature mortality of children. This effect was estimated in meta-analyses to have the potential to decrease the mortality of deficient preschoolers by up to 30 per cent. This led to a vast expansion of interest in the vitamin. Helen Keller International currently has programmes in over 25 countries (not all including vitamin prevention and control programs). In 1986-87 the author had also been with HKI as Country Director of the Nutritional Anaemia Prevention Programme with the Institute of Public Health Nutrition of the Government of Bangladesh.

After his time in Bangladesh, the author later became Regional Adviser in Nutrition for the Western Pacific Regional Office of the World Health Organization, with early involvement in the iodine deficiency disorders (IDD) prevention and control programme in China and other countries in the region, as well as working with countries on plans to prevent and control iron deficiency anaemia (IDA), vitamin A deficiency disorders (VADD), and in developing national plans of action for nutrition (NPANs). Subsequently he became Director of the large fully-USAID funded Project, OMNI (Opportunities for Micronutrient Interventions). Following the USAs commitment to the international goals (to be discussed in the course of the thesis), the OMNI Project was USAID's response to these goals, with potential funding of $US25 million over the 5 year contract (managed by John Snow Inc. in Washington, DC, USA).

He was subsequently UNICEF Senior Adviser, Micronutrients at UNICEF Headquarters in New York, USA, and is currently Acting Chief of the Nutrition Section, and Senior Adviser, Child Survival and Development. He is concurrently Visiting Associate Professor at the Institute of Human Nutrition, Columbia University, New York, USA, Adjunct Associate Professor with the Nutrition Program, University of Queensland, Australia, and visiting post-graduate Fellow at the School of Human Life Sciences at the University of Tasmania. The thesis will draw on all these experiences, perspectives and the access they gave to relevant individuals and documents, and all of which inform the content.

1.3 Background: the problem

Micronutrient malnutrition is a serious threat to the health and productivity of more than 2,000 million people worldwide despite being largely preventable (WHO 1995, MI/UNICEF 2003). Because of their high prevalence and close association with childhood illness and mortality, the three micronutrient deficiencies of current greatest public health significance are iron, vitamin A and iodine (FAO/WHO 1992), although zinc is receiving increasing attention (Hotz & Brown 2004). Folate deficiency is widespread, based on incidence of neural tube defects and low homocysteine levels (Brent & Oakley 2006), although the folic acid to correct these conditions may also be working partly through a pharmaceutical effect. Vitamin B12 is thought to be more widespread than previously (Rogers et al. 2003). Other micronutrient deficiencies such as thiamin, riboflavin and selenium are reported in Africa and Asia and Pacific regions, and less so in the Americas (Darnton-Hill, Cavalli-Sforza, Volmanen 1992, ACC/SCN 1992, Rayman 2002). Rickets continues to be described sporadically, for exmple in China (Cavalli-Sforza et al.1991) and Bangladesh (Welch et al. 1998), and is a significant public health problem in Mongolia and the Central Asian Republics. Specific deficiencies, for example selenium and vitamin D are reported from various countries such as New Zealand and Mongolia (Darnton-Hill 1995), or potentially dangerous excesses such as arsenic in much of the Indian sub-Continent and fluoride in China and elsewhere (FAO/WHO 2004). Women and children are more vulnerable to micronutrient deficiencies because of their added requirements for reproduction and growth (Calloway 1995), especially in low-income countries with poor diets and high disease burden. This gender disparity has specific implications for vitamin and mineral deficiencies programmes (Darnton-Hill et al. 2005a) and has also been suggested, at least in the case of anaemia, as one of the reasons for the low public health priority given to addressing iron deficiency despite the magnitude of the anaemia problem globally. Including clinical and subclinical forms, *vitamin A deficiency disorders* (VADD) have been identified globally at levels representing a public health problem in 70 countries and a likely public health problem in a further 30 (WHO 2004a) (see Appendix 2.1 after Chapter 2). Well over half of those with vitamin A deficiency (VAD) are found in Asia, notably South Asia (Mason et al. 2001) but also in China, particularly in minority populations (Long, Yang, Wang 1998) and Micronesia (Darnton-Hill, Cavalli-Sforza,

Volmanen 1992, Lloyd-Puryear et al 1989). Subclinical vitamin A deficiency is now recognized to be not uncommon in schoolchildren, adolescents and pregnant women in some settings (Bloem, de Pee, Darnton-Hill 1998, West 2002, West & Darnton-Hill 2007) and may have an important role in HIV (Semba et al. 1994) although that is currently still unclear (Fawzi et al. 2004a), and be a significant contributor to maternal mortality (West et al. 1999, West 2002).

The global population was estimated in a 2001 Report to be 75-140 million pre-school age children, with the upper range thought more likely (Mason et al. 2001). A more recent estimate is approximately 127 million with VAD (serum retinol<0.70µmol/L) (West 2002). More than 7.2 million pregnant women in the low and medium income countries are deficient in vitamin A (serum or breast-milk vitamin A concentrations <0.70µmol/L), with over 6 million women developing night blindness during pregnancy annually (West 2002). The total Asian and Pacific population with subclinical vitamin A deficiency is estimated to be about 47 million, with a resulting significantly increased risk of early mortality in children. Globally, over 4 million preschool children are estimated to have clinical signs of vitamin A deficiency (xerophthalmia) with resulting serious risk of blindness and early death. Approximately 3 million of these children are in Asia (Mason et al. 2001, West 2002). Although there has been notable success in controlling and preventing clinical vitamin A deficiency, at least as estimated through supplementation coverage (Dalmiya, Palmer, Darnton-Hill 2006), some countries, and particularly socially disadvantaged countries, still show levels in excess of the prevalence at which WHO defines there to be a public health problem (UNICEF/WHO 1994a).

The main causes of vitamin A deficiency in the developing world are insufficient dietary intake of vitamin A (from relatively expensive animal sources) and poor bioavailability of provitamin A sources (vegetables and fruits). Other important contributing factors include the increased requirements at certain stages in the life cycle; increased utilization of vitamin A during infection, especially measles; and socio-cultural factors such as intra-household distribution and gender (Sommer & West 1996, Bloem, de Pee, Darnton-Hill 1998, West & Darnton-Hill 2001, 2007, Ahmed & Darnton-Hill 2004, Webb, Nishida, Darnton-Hill 2007).

Globally, the *iodine deficiency disorders* (IDD) were a significant public health problem in 118 countries (WHO 1995) due to iodine-poor environments, with a total of 740 million people affected by goitre worldwide, with 20 to 30% of these in Africa and Eastern Mediterranean (WHO/UNICEF/ICCIDD 1993, Mason et al. 2001, WHO/UNICEF/ICCIDD 2001). The WHO database has now moved to the more reliable measure of urinary iodine excretion and estimates the figure of those with insufficient iodine intake to be approximately 1,989 millions in 54 countries, with WHO having no data on 66 countries out of 126 countries globally (WHO 2004a). Iodine deficiency is the commonest cause of preventable intellectual impairment in the world today, as well as having negative effects on the reproductive experience of women and on economic productivity (Bleichrodt & Born 1994, Hetzel & Pandav 1997, Hetzel et al. 2004). Children born in iodine-deficient areas have been estimated to lose the potential of at least 10 IQ points compared to those born in iodine-replete areas. A report from Indonesia has raised the possibility of a significant impact on deaths in infants, as iodine supplements given to infants of 6-10 weeks halved the risk of dying in the 4 months following supplementation (Cobra et al. 1997).

In the Asia Pacific region alone, the total population at risk is over 900 million and in 1990, 317 million were estimated to be goitrous (WHO/UNICEF/ICCIDD 1993). The loss of intellectual potential and economic productivity is therefore enormous (Hetzel et al. 2004). In the Asia-Pacific region in the early 1990s, there were over 7 million cretins. In Asia, just by sheer size, Bangladesh, China, India and Indonesia together account for over 50% of the world's population at risk of IDD (WHO/UNICEF/ICCIDD 1993). Nearly all the countries in Asia have a problem to a greater or lesser degree. There are fewer problems in the Pacific although it has been reported in Fiji and remains a significant problem in the highlands of Papua New Guinea. Both Australia, particularly around Canberra and the eastern coast and in Tasmania, and New Zealand previously had significant problems. Prevalences have been recently identified as increasing again in Australia, New Zealand and the USA (Guttikonda et al. 2002, Eastman 2006). Europe, despite being the first country to recognize the aetiology of the problem, and Switzerland, the first to iodize salt in one Canton, still have a significant problem (Andersson et al. in press).

Conservative estimates indicate that 1,500-2,000 million people are anaemic world-wide, mainly from *iron deficiency anaemia*, with perhaps over 90% of these in the developing world, mainly South Asia and Africa (DeMaeyer et al. 1989, Stoltzfus 2001b, McLean et al. 2007). More recent estimates suggest there has been little change in the prevalence levels (MI/UNICEF 2003, Darnton-Hill, Paragas, Cavalli-Sforza 2007). Relatively recent global estimates of iron deficiency anaemia have ranged from 600 to 2,000 million, with many more, perhaps twice this figure, iron deficient (WHO/UNICEF/UNU 2001, MI/UNICEF 2003). This averages to nearly 60% of all (both pregnant and non-pregnant) women in developing countries. For low income countries as a whole the average prevalences are 42% of non-pregnant women and 56% of those pregnant (MI/UNICEF 2003), although more recent figures from WHO show even higher figures in many countries, especially those of South Asia (McLean et al. 2007). Iron deficiency, the main cause of anaemia, is a major contributor to low birth weight, prematurity and maternal mortality (DeMaeyer et al. 1989, WHO/UNICEF/UNU 2001, Stoltzfus 2001). Iron deficiency anaemia (IDA) is even more prevalent in infants and young preschoolers, and while there have been no published global data on the prevalence of IDA in infants and children, in some sample populations prevalence reaches 70% or more (Mclean et al. 2007) e.g. over 95% in Pemba, Tanzania (Sazawal et al. 2006). It has recently been increasingly re-recognized as an important cause of cognitive deficit in this age group (Draper 1997). Iron deficiency also has a profound effect on productivity and hence has economic implications for countries in which it is a significant public health problem (Aldermann & Horton 2007), with physical work capacity being reduced even in moderate anaemia (Scholze et al. 1997, Darnton-Hill, Paragas, Cavalli-Sforza 2007).

For pregnant women prevalences of anaemia range from 5% in Australia through approximately 30% for East Asia, over 50% for many of the countries of Africa, South-east Asia and much of the Pacific, to over 80% for parts of South Asia and in malarious areas in Africa and Asia (Helwig, Rivers, Mason 2004, Mclean et al 2007). In a survey in India, 62% of adolescent girls in urban areas were anaemic and 81% in rural areas (Gopalan 1993). In many high prevalence areas, the picture is worsened by other dietary factors (low intake of folate, vitamin A, vitamin B12), malaria, associated helminthic infection and other infections (including now HIV/AIDS), as well as congenital haemolytic disease such as sickle cell anaemia and thalassaemia (Darnton-Hill, Paragas, Cavalli-Sforza 2007). In some Asian countries, e.g. Lao PDR, Viet Nam and in parts of the Pacific, high prevalences of thalassaemia have been described. Up to

36% of women of north Indian origin in Malaysia with anaemia have megaloblastic anaemia due to congenital haemolytic disorders (Darnton-Hill, Cavalli-Sforza, Volmanen 1992).

In recent years, deficiencies of public health significance of folate have been recognized, and programmes fortifying with folic acid put in place in the USA (Oakley, Bell, Weber 2004). The prevalence is thought by some to be under-estimated in other parts of the world (FAO/WHO 2004, Brent & Oakley 2006). Likewise, the prevalence and significance of deficiencies of riboflavin (Fairweather-Tate et al. 1992), vitamin B12 (Rogers et al. 2003, Allen & Jones 2005) and selenium (Rayman 2002) are all felt to be under-appreciated. The global prevalence of multiple (two or more) deficiencies is thought to be from 10 to 25% in pre-school children (Mason et al. 2001) and higher in women living in poverty but differs greatly according to local diets and environments (Huffman et al 1998, Persson, Eneroth, Ekström 2004).

As much of the cost of delivering micronutrients to target populations is in the logistics, infrastructure and personnel, and the same populations are virtually almost always suffering from general undernutrition, and virtually never of just a single micronutrient, there is currently much interest in a multiple micronutrient approach to fortification and supplementation (and is implicit in dietary based approaches) (UNICEF/WHO/UNU 1999). There is also some scepticism about this approach and both of these views will be discussed in a subsequent chapter. However, it is zinc that has received most recent attention. Zinc is the subject of several meta-analyses of its impact in a range of infectious diseases and reproductive outcomes (Hotz & Brown for IZiNCG 2004). The estimated percentage of the population at risk of inadequate intake (as deficiency is so hard to measure accurately) has been estimated by IZiNCG in 2004 to be over 20% in 80 countries, with estimates of up to almost 70% in countries such as Tajikistan and over half the population in Bangladesh (Hotz & Brown 2004).

However, it is the deficiencies of the three micronutrients, vitamin A, iodine and iron, which remain major problems in the world today. This was recognized and acknowledged globally in December 1992, at the International Conference on Nutrition (ICN), where representatives of 159 countries and the European Community agreed to eliminate IDD and vitamin A deficiency as public health problems by the end of the

century (2000) and to substantially reduce the prevalence of iron deficiency anaemia (FAO/WHO 1992). In 1990 the World Summit for Children had established broader goals for the health and well-being of children. The nutrition goals, including those for the micronutrients, agreed to at this forum were echoed at the ICN (FAO/WHO 1992) and again in the Special Session on Children in 2002 by the goals of the 'World Fit for Children' decade plan of action (UNICEF 2002a). To achieve the Millennium Development Goals, progress will need to be made in alleviating the global burden of micronutrient deficiencies, although they are not specifically mentioned (UN 2006). Given this demonstration of apparent political will, how has micronutrient malnutrition been addressed thus far, and where is it going? It is hoped that this body of work will answer these questions.

Chapter Two

2.1 Introduction

The purpose of this chapter is to give some background to the micronutrients in order to better understand the importance of deficiencies. Primarily Vitamin A, and then, in somewhat less detail, iron and iodine, will be discussed. Because of the increasing public health attention being paid to other micronutrients now, such as zinc, the vitamins folic acid and vitamin B12, these will also be briefly discussed. The particular micronutrient will be discussed by function, structure, dietary sources, bioavailability, clinical manifestations and pathophysiology, and the epidemiology of the deficiency, as these all help direct the search for effective interventions. However, it is not the purpose of this the chapter to provide an exhaustive up-to-the date review of all aspects of each of the micronutrients. Recent reviews are available that do that e.g. for vitamin A (Ahmed & Darnton-Hill 2004, Solomons 2006, West & Darnton-Hill 2002, 2007), all to one degree or another building on the classics of Bauerfiend (1986) and Sommer and West (1996); for iodine and the iodine deficiency disorders, (Semba 2001) and Hetzel has relatively recently led an editorial team that updated the pioneering work of himself and others such as Stanbury (1994), Hetzel and Pandav (1996) and the global success story of universal salt iodization, in Hetzel et al. (2004); iron and the nutritional anaemias are the subject of a book in press edited by Kraemer and Zimmermann (2007) with a chapter by Darnton-Hill, Paragas and Cavalli-Sforza (2007) that again builds on earlier work by DeMaeyer et al. (1989) amongst others and more recently Yip (2001) in the excellent volume edited by Semba and Bloem (2001 and currently being updated) on 'Nutrition and Health in Developing Countries'. There has been an explosion of work on the public health aspects of zinc e.g. (Shrimpton (2001) and Hotz and Brown (2004) and folic acid in fortification and more general issues related to micronutrient malnutrition e.g in the WHO/FAO publications on fortification (2006) and more generally in vitamin and trace element requirements (FAO/WHO 2004) and in the nutrition series by the Nutrition Society, including 'Public Health Nutrition' edited by Gibney, Margetts, Kearney and Arab (2004). In the next chapter will be a discussion of delivery mechanisms, and in the chapter after that (chapter 4), programmes and policies, their implementation, and monitoring and evaluation, including indicators.

2.2 Vitamin A deficiency, epidemiology and consequences

Vitamin A deficiency is the cause of over a million premature deaths each year in children globally (WHO/UNICEF/IVACG 1995, West 2002), is the commonest cause of childhood blindness, and is also a likely contributing factor to several cancers (West & Darnton-Hill 2007). Xerophthalmia was a recognized public health problem in much of Europe until early last century. The public health significance of vitamin A deficiency has been redefined in the last fifteen years to include its impact on the deaths from infectious diseases in developing countries where vitamin A deficiency is frequently endemic. There has been tremendous progress in reducing the prevalence of the most severe manifestations of the disease (xerophthalmia and blindness) which are on the decline in all regions of the world (Mason et al. 2004). Although much remains to be done, several countries in Asia which previously had a public health problem of severe vitamin A deficiency (xerophthalmia) by WHO standards (WHO/UNICEF/IVACG 1995) leading to blindness and early mortality, have reduced their levels to a point where this is no longer the case. Nevertheless, subclinical vitamin A deficiency is still a problem of public health significance (West 2002). At the same time, widespread subclinical vitamin A deficiency has now been recognized in places such as Micronesia in the Pacific Ocean, and in much of Africa (WHO/UNICEF/IVACG 1995). The relative frequent occurrence in women during pregnancy and the possible consequences of that have only recently been widely documented, which much increases the recognized magnitude of the problem (West 2002).

2.2.1 Function

Vitamin A is involved in regulating numerous key biologic processes in the body, including morphogenesis, growth, vision, reproduction, and cellular differentiation and proliferation. Both humans and animals cannot survive without vitamin A which, as it cannot be synthesized in humans, must be provided from the diet in adequate amounts to meet physiologic needs. A deficiency state may arise with prolonged inadequate intake, often coupled with the high, normal demands imposed by rapid growth during childhood, pregnancy or lactation, or by excessive utilization and loss during infection (Sommer & West 1996).

The term ‘vitamin A’ is a generic descriptor that refers to fat-soluble compounds with a chemical structure of retinoids and biologic activity comparable to retinol, and includes retinol, retinyl esters (the dominant form in food), retinaldehyde, retinoic acid species, and other vitamin A-active metabolic intermediates (Kaul & Olson 1998). Retinoic acids (all-trans and 9-cis) are irreversible metabolites of retinol that can fulfill some functions of vitamin A, such as controlling cellular differentiation, but not other functions, such as maintaining rod or cone vision. Vitamin A-active compounds are a subset of a much larger family of “retinoids” that share a common, monocyclic chemical structure.

Vitamin A in the diet is from preformed vitamin A in animal foods, and carotenoids (provitamin A) from plant sources. Dietary sources of preformed vitamin A (as esters) include animal foods such as liver, fish liver oils, butter, cheese, milk fat, egg and, increasingly, a large number of vitamin A-fortified, processed foods such as ready-to-eat cereal, snack foods, beverages and other non-fat dairy products (West & Darnton-Hill 2007). Approximately 50 of some 600 known carotenoid pigments are fat-soluble, yellow-orange “provitamin A” compounds that can be bioconverted to retinol and other vitamin A compounds following uptake and absorption in the intestinal mucosa. Provitamin A carotenoids are found in yellow fruits and vegetables, such as ripe papaya and mango, carrot and yellow sweet potato, dark green leafy vegetables (embedded in green chloroplasts) and egg. The vitamin A content in food, as found in standard food composition tables, is usually expressed as micrograms of retinol equivalents, or RE, which represents the biologic activity of 1 µg of all-trans retinol (NRC 1989). ß-carotene is the most ubiquitous and efficiently converted provitamin A carotenoid in food. It has long been held that ß-carotene in food is converted to retinol at a ratio of ~6:1, representing 1 RE per 6 µg of ß-carotene. However, recent research suggests that this ratio may be much larger and variable, in the order of ~12:1 for ß-carotene derived from ripe, yellow fruit and ~26:1 for ß-carotene derived from vegetables such as green leaves and carrots (de Pee et al. 1995, de Pee et al. 1998, West & Castenmiller 1998) and these considerations were taken into account in the WHO/FAO Report on vitamin and trace element requirements (FAO/WHO 2004). Other common provitamin A carotenoids, that are estimated to be half as efficient as ß-carotene in their conversion to vitamin A, include α-carotene, ß-cryptoxanthin and zeaxanthin.

2.2.2 Clinical manifestations and pathophysiology

Prolonged vitamin A deficiency will result in clinical eye signs, representing the more severe manifestation of the deficiency. An estimated 3 million young children globally have xerophthalmia (from the Greek *xeros* = drying; *ophthalmia* = of the eye) (Sommer & West 1996), the ocular consequences of vitamin A deficiency that include night blindness (XN), conjunctival xerosis (X1A), Bitot's spots (X1B), corneal xerosis (X2), ulceration (X3A) or necrosis (X3B, or keratomalacia). In the early 1980s, it was estimated that a half-million children were developing corneal xerophthalmia each year in South and Southeast Asia alone (Sommer et al. 1981). Approximately half of all corneal cases lead to blindness and of these blinded children; half will die within 6 months (Sommer 1982). Vitamin A deficiency remains the most common, preventable cause of childhood blindness in the world (Sommer & West 1996).

Clinical signs include the earliest, specific clinical manifestation of vitamin A deficiency of night-blindness (XN). Lack of vitamin A disables the visual cycle, resulting in poor vision in dim light that, if sufficiently severe, results in night blindness. Typically, a history of night blindness can be elicited using a local term for the condition, often translated as "chicken eyes" (which lack rods and, thus, night vision) or "twilight" or "evening" blindness (Sommer & West 1996). A history of night blindness is associated with low-to-deficient serum retinol concentrations in preschool-aged children (Sommer & West 1996) and pregnant women (Christian et al. 1998b). Nutritional and disease conditions that could contribute to night blindness and result in its being more prevalent in South Asia (e.g., zinc deficiency, wasting, anemia, infection), may partially blur its relationship with serum retinol compared to groups in Southeast Asia (Christian et al. 1998b). Eliciting night blindness in children can be difficult due to social, language and age constraints (rarely is it reliable under two years of age) and, not surprisingly, it has been found that the condition is more clearly identified in women than children (Katz et al. 1995).

Conjunctival Xerosis with Bitot's spots (X1B). Vitamin A deficiency leads to a keratinizing metaplasia of mucosal surfaces of the body, including the bulbar conjunctiva. In chronic deficiency, xerosis of the conjunctiva (X1B) appears as a dry, non-wettable, rough or granular surface, best seen on oblique illumination from a hand-light (Sommer 1982). Histologically, the lesions represent a transformation of normal,

surface, columnar epithelium, with abundant mucous-secreting goblet cells, to a stratified, squamous epithelium that lacks goblet cells. In advanced xerosis, grey-yellow patches of keratinized cells and saprophytic bacilli called “Bitot’s spots” (XB) may aggregate on the surface, temporal to the limbus and, in more severe cases, on nasal surfaces as well (Sommer 1995). Corneal xerophthalmia (X2) represents an acute decompensation of the corneal epithelium and is a sight-threatening medical emergency as can rapidly lead to ulceration and necrosis and irretrievable loss of vision in that eye (X3A/X3B).

2.2.3 Outcomes of vitamin A deficiency other than eye disease

***Poor Growth**:* Field trials have shown mixed effects of vitamin A on child growth. Several have failed to find an overall effect of vitamin A supplementation on weight or height gain, although a few have observed increases in arm muscle area (Sommer & West 1996) reflecting a possible shift toward greater lean body mass with vitamin A supplementation. Others have observed increments in linear but not ponderal growth, ponderal but not linear growth, or subgroup increments on both aspects of growth (Sommer & West 1996). Additional studies and stratified analyses suggest, however, that vitamin A can improve growth in children for whom vitamin A deficiency is likely to be growth limiting (West & Darnton-Hill 2007). Protein adequacy is a prerequisite for optimal transport and utilization of vitamin A. As most retinol transport is dependent on protein adequacy, serum retinol levels are depressed in the presence of wasting protein-energy malnutrition (Sommer & West 1996, Ahmed & Darnton-Hill 2004).

***Infectious morbidity**:* Vitamin A deficiency and infection interact within a “vicious cycle” (Scrimshaw 1966), whereby one exacerbates and increases vulnerability to the other. The bi-directional relationship complicates frequent cross-sectional evidence of depressed plasma retinol levels with diarrhoea, acute respiratory infections, measles, malaria, HIV/AIDS and other infectious illnesses (Stoltzfus et al. 1993, de Francisco et al. 1994, Sommer & West 1996). Prospective studies have shown that infection can induce vitamin A deficiency through a variety of ways, depending on the cause, duration and severity of infection and vitamin A status of the host at onset. Serum retinol may be depressed following infection because of decreased dietary intake or absorption due to diarrhea or intestinal pathogens, impaired or accelerated hepatic depletion of retinol reserves, increased retinol utilization by target tissues or increased urinary losses

associated with the acute phase response (Sommer & West 1996). Hyporetinolaemia adversely affects immune competence, which would then be expected to exacerbate or predispose children to infection (Semba 1994).

***Infection**:* Preschool children with mild xerophthalmia have been observed to incur a 2-3 fold higher risk of incident respiratory infection and diarrhoea compared to non-xerophthalmic controls (Sommer & West 1996). Thai children with serum retinol <0.35umol/L, representing severe biochemical deficiency, were 4 times more likely to develop respiratory infection in the subsequent three months than children with a normal serum retinol concentration (>0.70umol/L) (Bloem et al. 1989). Severe infection acutely decompensates vitamin A nutritional status and so can precipitate xerophthalmia. Indeed, in a prospective study in Indonesia, preschoolers with either diarrhoea or acute respiratory disease were twice as likely to have developed xerophthalmia in a subsequent 3-month period than healthier children, and measles and other severe, febrile illnesses are frequently reported to precede corneal xerophthalmia (Sommer & West 1996)

2.2.4 Excess

A brief discussion of excess is important, as concern about the risks of vitamin A supplementation has not infrequently become an issue with countries deciding on adopting prevention and control programmes. In general, the risk is over-stated. There are, however, recognized toxicities, as well as the more commonly seen transient side effects. The latter are thought to not have long-term consequences (Humphrey & Rice 2000). Several reviews of the topic are available (Bauernfeind 1986, McLaren et al. 1993, Olson 1996, FAO/WHO 2004). Most interestingly, hypervitaminosis A has been known through the traditions of the Inuit and others, including Artic explorers, who learnt not to eat polar bear or seal liver because of the extremely high vitamin A content (or indeed the livers of their huskie dogs in the case of some explorers with sometimes fatal results). Both acute and more commonly chronic toxicity have been described. In the former, this might be rightly called side effects of the ingestion of several hundred thousand international units of vitamin A leading to a rise in intracranial pressure, with vomiting, headache, drowsiness and papilloedema. Spontaneous recovery without residual damage usually follows without damage on stopping the vitamin (McLaren et al.

1993). Careful studies and follow-up of infants has demonstrated no long-term effects of the raised intracranial pressure (Humphrey & Rice 2000).

Congenital malformations in the foetus of mothers receiving large doses of vitamin A during the organogenetic period in utero are well-recognized in animals. While only clinical anecdotes are reported in humans, women receiving vitamin A analogues for treatment of severe acne has produced characteristic birth defects in a number of women (Rosa, Wilk, Kelsey 1986). Chronic toxicity over a period of months or years leads to the insidious onset of headache, loss of hair, dry and itchy skin, hepatosplenomegaly, and bone and joint pains (McLaren et al. 1993). Hypercarotenosis results from the prolonged ingestion of large amounts of carotenoids, often as carrot juice. Yellow or orange colouration of the skin is especially prominent on the nasolabial folds, forehead, axillae and groins and on palms and soles. The condition appears to be quite harmless and does not lead to hypervitaminosis A (McLaren et al. 1993).

2.2.5 Epidemiology

However, it is the deficiency state that is overwhelmingly the more important in public health terms and so the rest of the overview is directed at vitamin A deficiency and the resulting disorders. Vitamin A deficiency, as xerophthalmia, has been known to plague humankind over the past 3500 years (West & Darnton-Hill 2001). Night blindness, and its treatment with foods now known to be rich in preformed vitamin A esters such as roasted ox, ass or beef liver, was reported from ancient Assyria, Egypt and Greece (Wolf 1996 as cited in West & Darnton-Hill 2001). Medical treatises from China, Europe, the Middle East and Southeast Asia throughout the first and second millennia documented the occurrence of night blindness and therapeutic value of animal liver. Clinical descriptions of corneal xerophthalmia first appeared in England in the 18th century, followed by additional reports in the 19th and early 20th centuries of its occurrence, association with infection and poor growth, and cure with animal and fish liver and oil products. Characterization of conjunctival xerosis with superficial accumulation of keratinized cells and bacilli organism, named “Bitot’s Spots”, was first described by von Hubbenet and, later, Bitot, in France in 1860. The need for, and existence of, indispensable accessory nutritional factors emerged in the scientific community in the late 19th century. In Japan in 1904 Mori drew attention to the inadequacy of rice and

barley-based diets of children with “Hikan” (a disease that included keratomalacia) and the condition’s rapid clinical response to cod liver oil (Wolf 1996 as cited in West & Darnton-Hill 2001). Xerophthalmia was still being reported in Europe early last century (Oomen 1976).

In the early 20th century “vitamines” were identified, led by figures such as Hopkins, Frank, Osborne and McCollum. Rat experiments conducted by McCollum and Davis and, at nearly the same time, Osborne and Mendel showed that the additions of small amounts of an ether soluble extract from butter, egg yolk or milk to the diets could promote growth, reduce morbidity and enhance survival. McCollum called this extract “fat soluble A” which was shortly thereafter renamed “Vitamine A”. The clinical relevance of the animal findings became quickly apparent. Bloch, a Danish paediatrician during World War I, observed how orphans subsisting on a fat-free milk, oatmeal and barley soup diet were at greater risk of keratomalacia, infection and poor growth, in ways that were similar to descriptions reported in animals by McCollum, compared to children whose diet included a modest amount of whole milk. With Wolbach and Howe’s classic description in 1923 of widespread metaplasia and keratinization of epithelial linings of the respiratory and genito-urinary tracts and glandular ducts in vitamin A-depleted animals, loss of the “barrier function” of epithelial linings became one plausible explanation for the associated decreased resistance to infection (historical sources cited in West & Darnton-Hill 2001). While animal experimentation continued, clinical studies in humans from the nineteen twenties through the forties continued to reveal associations between vitamin A deficiency or xerophthalmia and infectious diseases (Semba 1994, Semba 1999). The inverse relationship between febrile illness and plasma vitamin A concentration, now understood as part of the acute phase response to infection, and the potential therapeutic efficacy of vitamin A in reducing childhood measles fatality, puerperal fever in women, and other clinically relevant conditions (Semba 1999, West & Darnton-Hill 2001).

Epidemiologic studies since the 1950s have described the public health consequences, and benefits, of preventing vitamin A deficiency in human populations in the developing world. Clinical investigations by McLaren in Jordan and Gopalan and colleagues in India (cited in West & Darnton-Hill 2001) provided photographic and clinical details of conjunctival and corneal xerophthalmia and its interaction with protein-energy

malnutrition. In 1962, Oomen, McLaren and Escapini's 46-country FAO/WHO "survey" of national health and nutrition institutions for extant reports and data on xerophthalmia indicated the global significance of this problem throughout the developing world (Oomen, McLaren, Escopini 1964). Lack of population-based data and biases inherent in this type of data collection were appreciated. Nonetheless the study mobilized further surveys, research and commitment to prevent vitamin A deficiency and served as the forerunner of the current WHO classification system of countries at risk of vitamin A deficiency as a public health problem.

A national cross-sectional survey, a large, population-based, prospective study, and several hospital-based clinical studies of xerophthalmia among Indonesian children by Sommer and colleagues in the late nineteen seventies built on this earlier work and demonstrated aspects of causation, progression, risk factors and health consequences of childhood xerophthalmia and vitamin A deficiency in low income countries. Reports from this work, in the early eighties, showed that non-blinding, mild xerophthalmia (night blindness and Bitot's spots) was associated with markedly increased risks of preschool child mortality (Sommer et al. 1983), diarrhea and respiratory infections (Sommer, Katz, Tarwotjo 1983).

While the main causes of vitamin A deficiency in the developing world are insufficient dietary intake of vitamin A and poor bioavailability of provitamin A sources (vegetables and fruits), other important contributing factors include the increased requirements at certain stages in the life cycle; increased utilization of vitamin A during infection, especially measles; and socio-cultural factors such as intra-household distribution and gender (Sommer & West 1996, Bloem, de Pee, Darnton-Hill 2005, Webb, Nishida, Darnton-Hill 2007). The epidemiology of vitamin A deficiency relates to the distribution of deficiency by location, person and time and identifies risk factors that may be proximal and causal, for example diet, care and morbidity, less proximal or indirect (e.g., SES, parental education) (Ahmed & Darnton-Hill 2004, West & Darnton-Hill 2007).

Between 125 and 250 million preschool aged children are likely to be vitamin A-deficient, with high-risk populations located mostly in the peri-equatorial regions of the world (Figure 5.2 in Chapter 5) (MI/UNICEF 2003), with the most recent estimation being approximately 127 million with vitamin A deficiency (serum retinol<0.70μmol/L) (West

2002). More than 7.2 million pregnant women in the low and medium income countries are estimated to be vitamin A deficient (serum or breast-milk vitamin A concentrations <0.70μmol/L), with more than 6 million women developing night blindness during pregnancy annually (West 2002). The geographic distribution roughly parallels ecological indices of poverty and malnutrition (UNICEF 1998a, MI/UNICEF 2003, UNICEF 2007a). While most deficiency is "subclinical", apparent only by biochemical (e.g., serum retinol concentrations), histopathologic (e.g., abnormal conjunctival cytology) or functional (e.g., dark adaptation) test data, this nevertheless represents a severe threat to child health globally. There has been a recent move to use the term vitamin A deficiency disorders (VADD), analogous to the 're-positioning' of iodine deficiency disorders as IDD (iodine deficiency disorders) to reflect that this is a continuum and because the prevalence of 'clinical' signs require such large numbers due to low prevalence traditionally, and increasingly lower all the time, in virtually all countries in which it is a problem (Ramakrishnan & Darnton-Hill 2002). Based on serum retinol measurement, a population prevalence of deficient concentrations (< 0.35 μmol/L) of greater than 5% among preschool-aged children identifies vitamin A deficiency as a public health problem. More sensitive criteria could also be applied to classify a country or region (e.g., using a prevalence cutoff of 10% for serum retinol < 0.70 μmol/L).

Vitamin A deficiency has long been known as an "anti-infective" vitamin, (Semba 1999). Decades of animal experiments have shown that progressive vitamin A depletion leads to poor growth, weight loss, infection and death, often before eye signs develop (Sommer & West 1996). The regulatory roles of vitamin A in maintaining epithelial cell differentiation and function and immune competence have provided biologic plausibility to its importance in decreasing severity and mortality of infectious diseases (Semba 1994, Ross 1996, Beaton et al. 1993, Sommer & West 2004). Early work in Indonesia, particularly by Oomen and colleagues recognized the high levels of vitamin A deficiency in children of the developing world and its impact on childhood blindness (Oomen & ten Doesschate1973).

Since 1986 eight population-based vitamin A-child mortality intervention trials, enrolling more than 165,000 children, have been conducted in Southeast Asia (Sommer et al. 1983, Muhilal et al. 1988) and South Asia (Rahmathullah et al. 1990, Vijayaraghavan et

al. 1990, West et al. 1991, Daulaire et al. 1992) and Africa (Ghana VAST 1993, Fawzi et al. 1993). Results of meta-analyses based on these trials showed that, in areas of endemic vitamin A deficiency, mortality of children 6-71 months of age can be reduced, on average, by 23% to 34% following vitamin A supplementation (Beaton et al. 1993, Glasziou & Mackerras 1993, Tonascia 1993, Fawzi et al 1997), depending on studies included and analytic approaches taken in each meta-analysis. This considerable public health effect can be partly explained by an ability of vitamin A to lower case fatality from measles by almost half, as observed in field trials and hospital-based measles trials (Sommer & West 1996, Ellison 1932, Barclay, Foster, Sommer 1987, Hussey & Klein 1990), mortality from severe diarrhoea and dysentery, by approximately 40% (Rahmathullah et al. 1990, West et al. 1991, Daulaire et al 1992, Arthur et al. 1992) and, based on morbidity findings from a recent supplementation trial, possibly falciparum malaria (Shankar et al. 1999). Combining mortality effects with data on the prevalence of vitamin A deficiency, it has been estimated that 1.3 to 2.5 million early childhood deaths each year can be attributed to underlying vitamin A deficiency (Humphrey, West, Sommer 1992)

Despite the wide evidence and meta-analyses, West and others have pointed to two apparently incongruent observations: in contrast to evidence relating vitamin A deficiency to respiratory tract compromise and infection (Sommer & West 1996), vitamin A supplementation has not had a consistent effect in reducing the incidence, severity or mortality of acute lower respiratory infection in children (West & Darnton-Hill 2001). Secondly, vitamin A supplementation of infants under six months of age, either provided directly (Daulaire et al 1992, West et al. 1995, WHO/CHD 1998) or indirectly through maternal provision (Katz et al. 1999), has generally not shown a survival benefit in early infancy, which concurs with a lack of effect on early infant diarrhoeal and respiratory morbidity (WHO/CDH 1998). There have been two exceptions to date: a 64% reduction in infant mortality observed among Indonesian infants randomized to receive 50,000 IU of vitamin A within 24 hours after birth (Humphrey 1997) and a study from India but where the impact was only in children of low birthweight (Rathmatullah et al. 2003). Although apparently safe (WHO/CHD 1998), the inconsistency in the effect of vitamin A supplementation on survival in early infancy, in populations at varying risk, is still not resolved at present. This is hampering the ability to make recommendations for infants less than 6 months, which would have programmatic advantages added on to routine

immunization, although WHO is planning a further consultation on vitamin A supplementation guidelines this year (2007) (which has now been delayed until after a meta-analysis by WHO on neonatal dosing following further reports on possible survival benefit of a neonatal dose of 50,000 IU).

The influence of vitamin A on survival has relatively recently been extended to the reproductive years of women. An estimated 10-20% of women living in rural, malnourished populations of South Asia experience night blindness during pregnancy or lactation (Bloem, de Pee, Darnton-Hill 1998, Katz et al. 1995, Christian et al. 1998a). Beyond being symptomatic of vitamin A deficiency, its occurrence during pregnancy appears to reflect a state of chronic vitamin A deficiency, anemia and wasting undernutrition, increased risk of infection and reproductive morbidity (Christian et al. 1998a,b, 2000), and is associated with lower maternal survival during the first 1-2 years following delivery (Christian et al. 2003). Therefore, it seems likely that in malnourished (non-HIV positive) populations of women of child-bearing age, improved vitamin A intake, through supplementary or presumably dietary means, at recommended levels, may substantially reduce risk of mortality related to pregnancy (West et al 1999), although this still remains to be confirmed (but was not in a large study in Bangladesh (West personal communication 2007).

A strong, dose-risk gradient exists between maternal serum retinol and vertical transmission of HIV and cervico-vaginal shedding of HIV DNA (Semba & Gray 2001), suggesting that maternal vitamin A deficiency may affect pregnancy outcomes in HIV+ populations. To-date, however, vitamin A supplementation of HIV+ pregnant women in populations has shown little effect on outcomes such as low birth weight or perinatal mortality (Fawzi et al. 1998), or in interrupting transmission of HIV from mother to infant (Coutsoudis et al. 1995, Semba & Gray 2001). This recent evidence of relatively high prevalences in women of the developing world, and the health impact of this, has encouraged many in international public health to examine new paradigms in the prevention and control of vitamin A deficiency (Bloem, de Pee, Darnton-Hill 1998). Recent evidence has suggested that vitamin A may have a negative, or at least, neutralizing impact, in HIV positive women. A recent study with multimicronutrients not containing vitamin A, compared with those containing vitamin A actually appeared to

neutralize the impact in delaying progression to AIDS seen with the non-vitamin A-containing multimicronutrients (Fawzi et al. 2004a).

Vitamin A deficiency is a major public health problem in approximately 70 low income countries (WHO 2004b) largely spanning peri-equatorial regions of the world, where vast numbers of rural and peri-urban poor are exposed to inadequate dietary vitamin A and frequent infections. Another 30 have vitamin A deficiency as a likely public health problem with 23 identified as not having a problem and 69 with no recent data available (WHO 2004b) (Annex 2.1). The extent and severity of deficiency also appears most widespread where diets generally lack preformed vitamin A; for example, across large areas of South and Southeast Asia, and Sahelian and sub-Saharan Africa. Table 2.1 shows the general distribution, although depending on the method of extrapolating from subnational figures and other methodological differences, total numbers range from 125 million (West 2002) to 250 million (WHO/UNICEF/IVACG 1995, although the latter is generally thought to be too high.

TABLE 2.1: Global vitamin A deficiency (Mason et al. 2004)

Populations with:	Clinical signs		Subclinical[1,2]	
	Millions	%	Millions	%
UNICEF Region				
South Asia	1.58	0.95	32.3	19.2
East Asia & Pacific	0.40	0.25	14.8	9.1
Latin Am. & Caribbean	0.12	0.24	4.7	9.0
East. & South. Africa	0.53	1.06	10.0	20.0
West &Central Africa	0.45	0.87	9.4	18.1
Mid.East & North Africa	0.12	0.27	4.2	9.8
Total	3.30	0.63%	75.0	14.6%

1 (serum retinol<0.7µmol)
2 lower figure of estimated range

Vitamin A deficiency tends to cluster within countries with affected populations sharing common dietary patterns and other ecologic exposures, such as poor development and health infrastructures, strong seasonal fluctuation in food availability, low SES and so forth (West & Darnton-Hill 2007). The clustering intensifies within smaller groups, with population-based surveys in Africa (Malawi and Zambia), South Asia (Bangladesh and Nepal) and Southeast Asia (Indonesia) revealing a consistent 1.5 to 2.0 fold risk of xerophthalmia among children in villages where other children have the condition (Cohen et al. 1985, Katz et al. 1993, Sommer & West 1996). More striking is a 7 to 13-fold higher risk of having, or developing xerophthalmia, among children whose siblings have the condition, compared to children whose siblings are non-xerophthalmic (Katz et al. 1993). Children with xerophthalmia should not only be treated but action also taken with regard to the increased risk to siblings, household and the wider community.

2.2.6 Proximal causes

Vitamin A deficiency, as a public health problem, results from a chronic, dietary insufficiency of vitamin A, either preformed or from precursor carotenoids. It often occurs in association with protein-energy malnutrition, other micronutrient deficiencies and, as part of a “vicious cycle” with infection, in which one exacerbates and increases vulnerability to the other.

Even in affluent populations, newborns are normally born with low liver stores of vitamin A that increase rapidly after approximately 3 months of age throughout the preschool years, presumably reflecting dietary sufficiency from breast milk and complementary foods to promote storage of vitamin A in relation to normal requirements for growth and other needs. In malnourished societies, however, liver vitamin A stores may fail to accumulate beyond early infancy. This may be due, in part, to a combination of low breast milk vitamin A concentration, which is often half that of breast milk from well-nourished populations of women (Sommer & West 1996). Still, breast milk provides a critical dietary source of vitamin A that may protect children from xerophthalmia (Brown et al. 1982). In Malawi, accelerated weaning involving both premature introduction of complementary foods (at 3 vs. 4 m of age) and early cessation of breast-feeding was associated with increased risk of preschool xerophthalmia (West et al. 1986).

The mix of complementary foods in the household diet offered to infants after reaching six months can modify or even eliminate the excess risk of xerophthalmia associated with the loss of breast milk from the diet. In Indonesia, where no association existed between breast feeding and xerophthalmia in the preschool years, children not routinely given milk, egg, yellow fruits and vegetables, dark green leaves or meat/fish in the first 12 months of weaning were approximately 3 times more likely to be xerophthalmic than matched-control children given these foods (Mele et al.1991). Similarly, in Nepal, protective odds ratios against xerophthalmia in the preschool years ranged from 0.09 to 0.41 for regular (> 3 x per week) consumption of meat, fish, egg and mango in the first two years of life. Feeding histories of younger siblings in the first two years of life were similar to the cases and controls in the study (West et al. 1999), reflecting a chronically poor diet in high-risk households. Numerous epidemiologic studies provide the basis for a progression of complementary feeding that appears to guard children from xerophthalmia through the preschool years (West & Darnton-Hill 2001). Intake of sweet, yellow fruit (mango and papaya) are strongly protective in the second and third years of life. As the influence of breast milk weakens, dark green leafy vegetables appear strongly protective from the third year onward (West & Darnton-Hill 2007). After infancy, routine consumption of animal-source foods with preformed vitamin A (egg, dairy products, fish, and liver) is highly protective (Blankart 1967, Cohen et al. 1985a, Stanton et al. 1986, De Sole, Belay, Zegeye 1987, Pepping et al 1989, Mele et al. 1991, Rosen et al. 1994, Khatry et al. 1995, Bloem & Darnton-Hill 2001).

How and with whom children eat their meals may affect their risk of vitamin A deficiency. Detailed ethnographic studies have shown that rural Nepalese children are twice as likely to consume vegetables, fruits, pulses, meat or fish and dairy products when they share a plate with another relative during meals than when left to eat alone (Shankar et al. 1998). Among plate sharers, however, children with a known history of xerophthalmia (1-2 years previously) were 1.7 times more likely to share a plate at meal time with an adult than children from non-xerophthalmic households. Sharing a meal plate with a female of any age, on the other hand, was protective in its direction against childhood xerophthalmia. Paradoxically, this suggestive pattern of women assuring dietary adequacy for children in some cultures, may predispose mothers to vitamin A deficiency. In Nepal, for example, pregnant women with night blindness were approximately 50% as likely to consume vitamin A-rich foods, especially in the food-

scarce hot, dry and monsoon seasons as non-pregnant women (Christian et al. 1998a), and following the Indonesian economic crisis, mothers appeared to sacrifice their egg intake for their children (Bloem, de Pee, Darnton-Hill 2005, Webb, Nishida, Darnton-Hill 2007).

2.2.7 Those at risk

The profile of those populations at risk of vitamin A deficiency are extensively delineated in several reviews, perhaps most exhaustively in Sommer and West (1996). The following will briefly consider age, gender, and socio-economic status (and is based largely on West & Darnton-Hill 2001).

***Age**:* Based on hospital admissions data from Indonesia and Nepal, the risk of corneal xerophthalmia, which rarely affects more than 0.1% of a population even in high risk areas, appears to peak at 2 to 3 years of age (Sommer & West 1996, West 2002). This is often following recent weaning from the breast and sole dependence on a poor household diet, high risk of measles in non-immunized children, and persistent risk of diarrhea, wasting malnutrition and poor child care (Sommer 1982). Incidence of corneal disease declines beyond age three. The prevalence of mild xerophthalmia (XN and X1B), on the other hand, typically rises with age through the fifth year of life or beyond, irrespective of area of the world or age-specific rates of deficiency. This pattern may be reflecting a rise seen over time as children in high risk populations continue to be exposed to a poor diet (Mahalanabis 1991, West et al. 1986) and insufficient vegetables, fruits and animal products with adequate vitamin A content, while no longer having the benefit of breast-milk (West & Darnton-Hill 2007). Vitamin A deficiency also persists into adolescence, particularly among females of reproductive age (Ahmed, Hassan, Kabir 1997, Ahmed & Darnton-Hill 2004). This risk becomes most apparent during pregnancy when, in rural South Asia, 10 to 20% of women report being night blind (Katz 1995, Christian et al 1998a, Bloem, de Pee, Darnton-Hill 1998,). Early reports from Africa suggest similar, high risks of night blindness among women of reproductive age (IVACG 1999).

Gender: Boys tend to show a higher prevalence of mild xerophthalmia than girls throughout the preschool and early school-aged years (Darnton-Hill et al. 2006, West & Darnton-Hill 2007, Webb, Nishida, Darnton-Hill 2007). The gender bias is less apparent

for subclinical (biochemical) deficiency (Kjolhede et al. 1995) and has not been observed with respect to severe, corneal xerophthalmia (Sommer 1995). Variation in how boys and girls tend to be fed across cultures is likely to dominate gender differences in risk (Solon et al. 1978,). Intrahousehold food distribution may well be another factor (Webb, Nishida, Darnton-Hill 2007, Darnton-Hill et al. 2007).

Socio-economic status (SES)*:* Poverty is strongly related to the risk of vitamin A deficiency, presumably by influencing adequacy of diet, hygiene and care among children. Studies across cultures reveal low socioeconomic status of households in which xerophthalmic children reside compared to non-xerophthalmic households, reflected by parental education, landholding, housing quality and hygiene, ownership of small assets and draft animals and history of child mortality (Khatry et al. 1995, Cohen et al. 1985, Mele et al. 1991, West & Darnton-Hill 2007). Not surprisingly, women with maternal night blindness also come from socioeconomically disadvantaged families (Christian et al 1998b). At the community level, high-risk villages marked by the presence of >1 child with xerophthalmia, tend to be poorer than those where no children have xerophthalmia (Khatry et al. 1995).

Seasonal trends and other fluctuations: Spring peaks in xerophthalmia were widely noted in early 20th century China, Europe and Japan, variably coinciding with the Spring growth spurt, changes in diet and the diarrhoea season (Sommer & West 1996). Drought increases risk of xerophthalmia (Oomen & ten Doesschate 1973). In rural South Asia, the incidence of xerophthalmia follows a predictable seasonality, waxing during the hot, dry season (March-June) and waning during the monsoon period (July-August) to a low level that is sustained beyond the major rice harvest months of January and February (Sinha & Bang 1976, West & Darnton-Hill 2007). The seasonal peak of night blindness and Bitot's spots is preceded by a period of high growth that follows the major harvest, which presumably draws on vitamin A reserves, and coincides with a period of low intake of fruits and vegetables and high incidence of diarrhoea and measles (Sinha & Bang 1973, 1976).

Risk of vitamin A deficiency can also shift over long periods of time, reflecting systemic improvements in economic development, food consumption, health services and environment. Though time trend data are absent, the past century has witnessed the

virtual disappearance of xerophthalmia from industrialized Western Europe, North America and Japan. More recently in Indonesia, the risk of potentially blinding vitamin A deficiency markedly decreased from the late 1970s to the early 1990s, reflected by a 75% reduction in the national prevalence of xerophthalmia (Muhilal et al. 1994) and a well-documented decline in xerophthalmia admissions to the Cicendo Eye Hospital in Bandung, in the presence of rising access represented by general pediatric admissions (Semba et al. 1995). Such progress, however, can be reversed in the presence of political and economic turmoil, as when xerophthalmia began to reappear in Indonesia following its economic collapse in the late 1990s (Bloem, de Pee, Darnton-Hill 2004).

2.3 Iodine deficiency disorders, epidemiology and consequences

The public health importance of iodine deficiency is that it is the most common cause of preventable intellectual impairment in the world. It is also important in terms of women's reproductive outcomes and probably infant mortality. The fact that infants born to mothers who are iodine deficient are likely to suffer intellectual impairment, even when there may be no clinical manifestations of cretinism (the most extreme manifestation) makes this extremely important both in community terms but also for national economic development. An estimate of iodine deficiency, or those suffering from iodine deficiency disorders (IDD) as assessed by goitre prevalence, was estimated globally at around 740 million in 1998 (UNICEF/WHO/ICCIDD 1999, Mason et al. 2001).

The prevalence of IDD was assessed by the presence of visible plus palpable goitre (the latter being somewhat unreliable as a measure) at about 20-30% in Africa and the eastern Mediterranean region (including Pakistan) while estimates for SE Asia were lower (MI/UNICEF 2003). More recent estimates use the more reliable urinary iodine excretion (UI) as goitre responds slowly to a change in iodine status (WHO 2004) (Table 2.2). The total goitre rate (TGR) should now only be used to make comparisons with earlier data (such as the WHO 1993 data) (WHO 2004b). The total number of the general population (extrapolated from school-age children studies using urinary iodine) is estimated in 2003 to have been nearly 2 billion (1,988,700,000) (WHO 2004b).

TABLE 2.2: Proportion of population and number of individuals in the general population (all age groups) with insufficient iodine (as estimated by urinary iodine levels) by WHO Regions in 2004 (WHO 2004).

WHO Regions	2004	
	Proportion (%)	Total numbers (millions)
Africa	42.6	260.3
Americas	9.8	75.1
South-East Asia	39.8	624.0
Europe	56.9	435.5
Eastern Mediterranean	54.1	228.5
Western Pacific	24.0	365.3
Total	35.2	1,988.7

2.3.1 Functions and structure

Iodine is a constituent of the thyroid hormones thyroxine and triiodothyronine- hormones that are essential for normal growth and physical and mental development (Hetzel 1993). Iodone's critical function (for the purposes of the public health control of IDD) is in the production and regulation of the thyroid hormones. Thyroid function is essential for normal growth and development. Thyroid hormone deficiency from any cause including severe iodine deficiency, leads to severe retardation of growth and maturation of almost all organ systems (Hetzel 1993, Delange & Hetzel 2004). The most familiar iodine deficiency disorder is goitre or the swelling of the thyroid gland in the neck. However, in the last 30 years or so, (not least because of the activities and advocacy of the International Council for Control of Iodine Deficiency disorders- ICCIDD), the understanding of iodine deficiency has gone far beyond goitre to encompass all the effects of iodine deficiency, including those on the foetus, neonate, the child and adolescent, and the adult (Hetzel et al. 2004).

Iodine exists in nature, in the soil and seas as iodide. Iodide ions are oxidized by sunlight to elemental iodine, which is volatile, so that every year some 400,000 tons escape from the surface of the sea. Iodine exists in the thyroid as inorganic iodine and the iodine-containing amino acids moniodotyronine (MIT) and diiodotyronine (DIT), thyroxine (T4), triiodothyronine (T3), polypeptides containing thyroxine and thyroglobulin.

Thyroglobulin is a glycoprotein (MW 650,000) with iodinated amino acids in a peptide linkage. It is the chief constituent of the colloid that fills the thyroid follicle and serves as the storage form of the thyroid hormones and contain 90% of the total iodine in the gland. It exists in the blood as thyroxine (T4), triiodothyronine (T3) and inorganic iodine. The level of inorganic iodine falls in iodine deficiency and rises with increased intake. T4 and T3 are mainly bound to the plasma proteins, with only about 0.5% free in human serum.

2.3.2 Dietary sources and intake

As noted, most of the iodine in nature is in the oceans where it has been since primordial times. Of the once more concentrated levels on earth, large amounts have been continuously leached from the surface soil by glaciation, snow and rain, and carried by wind, rivers and floods into the sea (Hetzel 1993). The deeper layers of soil, oil wells and natural gas effluents and deep water wells have iodine present, and so deep wells can be a major source. Plant foods are particularly likely to show reduced iodine content in deficient solids. Milk and meat are richer sources, while the best natural sources are seafoods. Cooking reduces the iodine content of foods, with over half of the iodine escaping during boiling, whereas only about a fifth is lost in grilling and frying (but which would destroy more of the vitamin A in the food).

The recommendation level for a population's mean intake of iodine is 100-150ug/day. Intakes range from 20-80µg/day in some parts of Africa to 2-3g in Japan (FAO/WHO 2004). It is currently recommended that infants have an intake of 15µg/kg/day reducing to 2µg/kg/day for adolescents (13+ years) and adults, increasing to 3.5µg for pregnant and lactating women (FAO/WHO 2004). The iodine requirement for pre-term infants is twice that of term infants (FAO/WHO 2004). In the presence of ingested dietary goitrogens, adult levels should be increased to 200-300 µg/day. These levels have important implications for the levels recommended for the fortification of salt with iodine, and more recently for supplementation (Untoro et al. 2007).

Iodine is readily absorbed, but only a half of other organic iodine compounds or the thyroid hormones themselves, are so readily absorbed, but more so from animal food sources. With a population's mean requirement amounting to 100-150ug/day, food sources rather than water intake are the more important contributors to iodine intake.

Where iodine deficiency occurs this will persist unless a supplement is given or the diet is made more varied with foods drawn from non-deficient areas, or where there is fortification of foods with iodine. This can be advertant as in iodized salt, or inadvertent as in the contamination of milk from iodophors used in cleaning cow's teats during milking. The major source in diets is from fortified foods, most commonly salt, but also sometimes water and some condiments.

Goitrogens are of secondary importance in the aetiology of endemic goiter, but important contributors in some settings. Some staple foods such as cassava, maize, bamboo shoots, sweet potatoes, lima beans and millet, contain cyanogenic glucosides which are capable of liberating large quantities of cyanide by hydrolysis (Bourdoux et al. 1980). Not only is the cyanide toxic, but also the predominant metabolite is the goitrogen thiocyanate. Only in the cassava plant are these found in the edible part of the plant and the additional effect of cassava on iodine deficiency has been demonstrated in non-mountainous Zaire (now the Democratic Republic of Congo) (Delange et al. 1982) and Sarawak, Malaysia (Maberley et al. 1983). Cassava is pre-eminently the staple of poverty as it will grow almost anywhere and provides carbohydrate as energy, although not much else and is cultivated extensively where it provides the major source of dietary energy for more than 200 million people living in the tropical regions.

2.3.3 Clinical manifestations and pathophysiology

The scientific basis for public health programmes has been concisely reviewed by Delange and Hetzel in the larger volume (Hetzel et al. 2004) and Semba (2004), building on earlier classic works such as that edited by Hetzel, Dunn and Stanbury (1987). Goitre has been noted and commented on since ancient times (Hetzel 1993). In the renaissance period in Europe, goitre was a not uncommon feature of paintings of the Madonna, especially in Italy. As noted, the importance of iodine deficiency now goes beyond goitre to the whole range of IDD. This re-positioning of the public health significance is further discussed in Chapter Four.

Iodine deficiency in the foetus due to maternal iodine deficiency leads to increased incidence of still-births, abortions, and congenital abnormalities. Endemic cretinism occurs when the iodine intake of the population falls below 25ug/day. Despite a

reduction in numbers since salt iodization has become more global, cretinism is still widely prevalent, affecting up to 10% of populations living in severely iodine-deficient areas of India (Kochupillai & Pandav 1987), Indonesia (Djokomoeljanto et al. 1983) and China (Ma Tai et al. 1982). In its most common form it is characterized by mental deficiency, deaf-mutism and spastic diplegia, referred to as the neurological type, in contrast to the less common 'myxoedematous' type characterized by hypothyroidism with dwarfism (Hetzel 1993). Mixed types can occur and have been described in China (Boyages et al. 1988). Cretinism was also particularly prevalent in Oceania (Papua New Guinea), parts of Africa and in the Andean region of South America (WHO/UNICEF/ICCIDD 1993, WHO 2004b).

In the neonate, there is an increased susceptibility as shown by the increased perinatal mortality. There is both permanent and transient neonatal hypothyroidism. The latter can be corrected by iodine supplementation, which if not done, will lead to abnormal neonatal brain growth and development (Hetzel 1993). In developing countries there is a much higher rate of neonatal hypothyroidism shown in blood taken from the umbilical cord (Kochupillai & Pandav 1987). It is related to severity of the iodine deficiency, as indicated by the prevalence of goitre and cretinism and level of excretion of iodine in urine.

Iodine deficiency in children is characteristically associated with goitre and the rate increases with age, reaching a maximum with adolescence (Hetzel 1993). Girls have a higher prevalence than boys. School children living in iodine-deficient areas have impaired school performance and lower IQs. Such populations are, however, also often poor, isolated, socially deprived with poor school facilities and poor general nutrition. Nevertheless, it has been convincingly shown that children born in iodine deficient areas have mental development that lags behind that of children born from non-iodine-deficient areas and the differences in psychomotor development only become apparent after the age of about 2.5 years (Bleichrodt & Born 1994) but can be picked up even when tested for at 10-12 years (Pharaoh & Connolly 1987).

The common effect of iodine deficiency in adults is goitre. Characteristically there is an absence of clinical hypothyroidism in adults with endemic goitre. Laboratory evidence

of hypothyroidism with reduced T4 levels is common, often accompanied by normal T3 levels and raised TSH levels (Hetzel 1987, Zhu 1983). The important public health focus, however, is to ensure woman of reproductive age are iodine sufficient, before pregnancy. The iodine-deficient adult is then treated as a clinical problem, including in some cases, as below, when exposed to IDD programmes.

Iodine-induced hyperthyroidism: Of note because of the possible negative impact on public health programmes (as well as individuals), the main hazard of iodization is transient hyperthyroidism, seen mainly in those aged over 40 years. It is caused by autonomous thyroid function resulting from long-standing iodine deficiency. In the long-term, as IDD is prevented, this therapeutic hyperthyroidism will disappear (Hetzel 1993). In the meantime, deaths have occurred and there are now guidelines to avoid this in iodized salt public health prevention and control programmes (Delange & Hetzel 2004, Semba 2004, FAO/WHO 2004, WHO/FAO 2006). The recent WHO report (2004b) had five countries with a median UI≥300µg/l, indicating an excessive iodine intake (UI between 200-299µg/l). Salt quality monitoring continues to be needed to be re-enforced in such countries.

2.3.4 Epidemiology

In general, as noted earlier, the older an exposed soil surface the more likely it is to be leached of iodine. The mountainous areas of the world such as the Andes, Himalayas, the European Alps and the mountains of China are particularly affected. Nevertheless, iodine deficient soils are far more widespread than this and iodine deficiency is likely to occur in all elevated regions subject to glaciations and higher rainfall, areas with run-of into rivers, as well as in flooded river valleys in Bangladesh, Burma (Myanmar) and India (Hetzel 1993). There is a cycle in which the iodine in the atmosphere is returned to the soil by the rain. This return, however, is slow and small compared with the original loss and repeated flooding ensures persistent iodine deficiency in the soil resulting in crops becoming iodine deficient, with the animals and humans dependent on local crops become iodine deficient. While European diets became more varied during the 19th Century, substantial areas of potential iodine deficiency remain in Germany, Italy, Spain and Switzerland, as well as in other more localized areas (Andersson et al. in press). Even though these countries have had salt iodization programmes for half a century in

some cases, there is a need for continuous surveillance. Australia and New Zealand have both had endemic areas, and again there is some indication that the problem may be resurfacing in some areas (Eastman 2006). The same is true globally, but disadvantaged areas and populations, especially those geographically isolated such as Tibet, continue to be most at risk, representing a challenge to reach with iodized salt, foods higher in iodine from other areas, or even supplementation.

As noted, there are thought to be about 740 million people worldwide affected by goitre and nearly 2 billion as having inadequate iodine nutrition as measured by urinary iodine (MI/UNICEF 2003, WHO 2004b). However, these figures are continuously under revision as original estimates were often based on subnational or old data. Earlier figures from WHO indicated an increase in prevalence, despite the undoubted impact of the widespread iodization of salt. This is presumed to represent an improvement in the accuracy of the numbers rather than a real increase. Nevertheless, it makes identifying trends and advocacy something of a challenge. About 87 national surveys of goitre have been carried out since 1970, but only for eight countries were repeat surveys conducted that were likely to be comparable (Mason et al. 2004). A comparison of the estimates for 1990 and 1998 indicates little change in the prevalence of IDD over this period. Again this most likely represents the increased effort to identify the deficiency in recent years. Trends will be discussed later in terms of iodization of salt and the presumed impact that this is having (Chapter Five). In the recent WHO report 66 countries had no data, and even though iodine deficiency is unlikely to be a problem in these countries, they should be checked (Andersson et al. 2005, WHO 2004b), but encouragingly there are now only 47 countries with a public health problem compared with 54 in 2004 and 126 in 1993 (draft document for World Health Assembly 2007). It also seems likely that the assessment of the World Fit for Children Goals by UNICEF, using the Multiple Indicator Cluster Surveys (MICS) and the Demographic Health Surveys (DHS) of USAID, will demonstrate little change globally, but great increases in USI coverage, in many more countries (Mangasaryan, personal communication 2007).

Overall, one third of the world's population has UI levels below 100µg/l indicating insufficient iodine intake and so are exposed to the risk of iodine deficiency. Using WHO regional groupings, the proportion of the population with UI <100µg/l ranges from 10% in the Americas to 60% in Europe (WHO 2004b). It should be noted a correlation

has been found between household coverage of iodized salt and a reduction in the prevalence of low iodine intake (UNICEF 2003, WHO 2004b). The proportion of households consuming iodized salt increased from 10% in the 1990s (WHO/UNICEF/ICCIDD 1999) to 66% in the year 2003 (UNICEF 2004). UNICEF uses the more advocacy friendly figures of 79 million newborns protected from losses in learning ability due to iodine deficiency, but that 41 million are still unprotected (UNICEF 2004).

2.4 Iron deficiency, iron deficiency anaemia and other nutritional anaemias

Conservative estimates indicate that 1,500 million people are anaemic world-wide, with perhaps over 90% of these in the developing world, mainly South Asia and Africa (DeMaeyer et al. 1985). Later figures give similar estimates of 600-700 million persons with iron deficiency anaemia (Beard & Stoltzfus 2001, FAO/WHO 2004), and one estimate suggests that underlying iron deficiency is approximately double this (Yip, Stoltzfus, Simmons 1996). Other figures estimate an affected 2 billion (Stoltzfus & Dreyfuss 1998) with young children and pregnant and post-partum women being the most commonly affected and most severely so (Stoltzfus, Mullany, Black 2004). Even more recent figures from WHO are soon to be published and unofficial prevalence figures are available in the recent review of nutritional anaemia (Kraemer & Zimmermann 2007), and seem slightly lower but emphasize the vast disparities between regions (McLean et al., 2007, Darnton-Hill, Paragas, Cavalli-Sforza 2007).

All the figures suggest that over half of all women in developing countries are anaemic. Iron deficiency, the main cause of anaemia, is a major contributor to low birth weight, prematurity and maternal mortality (DeMaeyer et al. 1989, WHO/UNICEF/UNU 2001, Beard & Stoltzfus 2001). Iron deficiency anaemia (IDA) is even more prevalent in infants and young preschoolers, and while there are only very recently global data on prevalence of IDA in infants and children, in some sample populations prevalence reaches 70% or more (SCN 2004, McLean et al. 2007). As indicated in the Chapter 1, nutritional anaemia, largely because of iron deficiency, remains the major nutritional problem facing the poorer nations. Even in more affluent countries, it remains a significant problem in certain, usually disadvantaged, groups. The recent WHO estimates give prevalence data for pre-school-age children, and non-pregnant and

pregnant women, according to information available and that were included according to pre-specified criteria (McLean et al. 2007). For infants and young children, the range is from 3.4% in North America to nearly two thirds (65.4%) in Africa. In women, the range is 7.6% in North America to 44.7% in Africa (non-pregnant), and for pregnant women, 4.7% to 55%. However, individual studies have identified far higher prevalences for infants and women, especially in South Asia that show for example 84.9% of pregnant women anaemic (<110g/l) with 13.1% having severe anaemia (<70g/l). In the 16 Districts of India surveyed (Toteja & Singh 2006), 90.1% adolescent girls had anaemia, with 7.1% having severe anaemia.

The recently published review volume on nutritional anaemia gives considerably expanded information from a largely public health perspective (Kraemer & Zimmermann 2007). Iron deficiency anaemia has recently been re-recognized as an important cause of cognitive deficit in this age group (Nestel & Davidsson 2002, Beard 2001), including in the very recent and potentially influential Lancet series on early child development (Walker et al. 2007). Iron deficiency also has a profound effect on productivity and hence has economic implications for countries in which it is a significant public health problem (McGuire & Galloway 1994, Ross & Horton 1998, Alderman & Horton 2007), with physical work capacity being reduced even in moderate anaemia (Scholze et al. 1997, Darnton-Hill, Paragas, Cavalli-Sforza 2007).

2.4.1 Structure

Iron is a d-block transition element that can exist in oxidation states ranging from –2 to +6, although in biological systems these are limited primarily to ferrous (+2), ferric (+3) and ferryl (+4) states (Beard 2001). There is an excellent concise overview by Lynch (2007). The interconversion of iron oxidation states is not only a mechanism whereby iron participates in electron transfer but also a mechanism whereby iron can reversibly bind ligands. Iron can bind to many ligands by virtue of its d orbitals, particularly oxygen, nitrogen and sulphur atoms. The main reactions are oxygen transport and storage, electron transfer and substrate oxidation-reduction. The activity of many of these enzymes decreases with tissue iron deficiency.

In the mammalian system, there are four major classes of iron-containing proteins carrying out such reactions: (i) iron-containing nonenzymatic proteins (haemoglobin and

myoglobin); (ii) iron-sulphur enzymes; iii) haem-containing enzymes; and, (iv) iron containing enzymes that are non-iron sulphur, non-haem enzymes. In the principal oxygen transport nonenzymatic proteins, haemoglobin and myoglobin, iron functions as a critical ligand for the binding of dioxygen. In iron-sulphur enzymes, iron participates in single-electron transfer reactions primarily in energy metabolism. In haem-containing enzymes, iron is bound to various forms of haem and participates again in electron transfer reactions when associated with various cofactors (e.g. cytochrome P450 complexes). The final group of iron-containing enzymes is a catch-all grouping in which iron is not bound to a porphyrin ring structure or in iron-sulphur complexes (Beard 2001). Haemoglobin is the most important (in terms of this discussion) iron-containing protein in red blood cells that carries oxygen from the lungs to cells throughout the body

2.4.2 Dietary sources and bio-availability

Iron in the diet is found in two main forms: haem from animal sources, and non-haem from plant sources. Bio-availability is considerably greater in the haem form. Haem sources are from meat and meat products and constitute about 1-2mg or 5-10% of the daily iron intake in most industrialized countries. In developing countries, the haem content of diets is usually negligible (FAO/WHO 2004). Non-haem sources are the main form of iron in all diets and occur in the diet from cereals, vegetables, pulses, beans, fruits etc.

Bio-availability refers to 'the degree to which iron is available for absorption in the gut and utilized for normal metabolic functions' (Nestel & Davidsson 2002). The two forms of dietary iron, haem and non-haem, utilize separate receptors on the mucosal cells (Hallberg, Sandström, Aggett 1993). After the uptake of haem iron into the mucosal cells, the porphyrin ring is split by the enzyme haemoxygenase within the cells and the iron is released. Non-haem and haem iron then have a common pathway and leave the cells in the same biochemical form, utilizing the same transfer system to the serosal side of the cell. It is probable that iron can only be absorbed into cells and pass the mucosal membrane in its ferrous form. Reducing substances, especially ascorbic acid, must therefore be present in the mucin layer of the mucosal cells for iron to be absorbed (Hallberg, Sandström, Aggett 1993).

The average absorption of haem iron in meat is about 25% (Hallberg, Brune, Rossander 1989). In contrast to non-haem iron the absorption is very little influenced by the iron status of the subject. For unclear reasons, haem iron that is not given together with meat is less well-absorbed (e.g. iron absorption from blood sausage is only about 2-3%) (Hallberg, Sandström, Aggett 1993). This is important as recent work from Kenya showed that meat supplementation improved growth, cognitive and behavioural outcomes in Kenyan children (Neumann et al. 2007). Haem iron can be degraded and converted to non-haem iron if foods are cooked at a high temperature for too long. Calcium appears to be the only other factor that influences the absorption of haem iron (Hallberg, Sandström, Aggett 1993).

Non-haem iron is much influenced by other dietary factors. Methodological considerations in the use of using two different radio-iron isotopes, internal standard meals and so on continue to confuse the accurate estimation of the actual absorption in different daily meals in many cultures and when taken under many conditions. The concept is of two pools of iron in the gastro-intestinal system and that iron absorption takes place independently from these two pools. However, even if the iron in one food item is well absorbed when given alone, if other foods in the same meal contain an excess of ligands inhibiting iron absorption (e.g. phytates), the absorption will be poor from all the iron compounds present in that meal. The non-haem iron absorption from a particular meal is thus not only dependent on the amount of iron but also, to a marked degree, the composition of the meal. The bio-availability can vary more than tenfold from meals with a similar content of iron, energy, protein and fat (Hallberg, Sandström, Aggett 1993). Just the addition of certain spices e.g. oregano, or a cup of tea, may reduce bio-availability by half or more. On the other hand, the addition of certain vegetables or fruits containing ascorbic acid may double or even triple the iron absorption, depending on the other properties of the meal and the amount of ascorbic acid present (Hallberg et al. 1993). As noted, many foods contain factors (ligands) which strongly bind iron and inhibit absorption. The most important inhibitors are phytates (inositol hexaphosphates), phenolic compounds, calcium, soy protein and so on (Table 2.3). There are other factors that enhance iron absorption such as ascorbic acid, consumption of meat and fish, and less consistently, organic acids such as citric acid, and sauerkraut, as well as other fermented vegetables, and even some fermented soy sauces (Hallberg, Sandström, Aggett 1993).

TABLE 2.3: Factors influencing dietary iron absorption (Hallberg, Sandström, Aggett 1993)

Haem iron absorption

- amount of haem iron present in meat
- content of calcium in meal
- Food preparation (time, temperature)

Non-haem iron absorption

- iron status of subjects
- amount of bio-available non-haem iron
- Presence of fortification and contaminant iron
- Balance between dietary enhancers and inhibitors

Factors enhancing iron absorption

- ascorbic acid
- meat, fish, seafood
- certain organic acids

Factors inhibiting iron absorption

- phytates
- iron-binding phenolic compounds
- calcium
- soy protein

2.4.2 Clinical manifestations and pathophysiology

The overt physical manifestations of iron deficiency include the generic symptoms of anaemia, which are tiredness, lassitude and general feelings of lack of energy. Clinical manifestations of iron deficiency can be accompanied by behavioural disturbances such as pica e.g. geophagia (eating of clay and dirt) and pagophagia (eating of ice). Neuromaturational delays are important and physiological manifestations of iron deficiency include reduced immunocompetence, thermoregulatory function, energy metabolism and exercise and work performance (Beard 2001, Lozoff 2006).

2.4.3 Function

Iron is essential for life, as part of the haemoglobin (Hb) molecule is essential for the transport of oxygen to cells of the body that supports bodily functioning, such as immune system functioning, neural functioning and also its role in muscle function and energy metabolism. Many biochemical processes need iron, besides the binding and transport of oxygen, including electron transfer reactions, gene regulation, and regulation of cell growth and differentiation (Beard 2001). Iron, besides being an essential nutrient is also a potential toxicant to cells and so the body has developed a highly complex set of regulatory approaches to meet the demands of the cells and body, while also preventing excess accumulation. The homeostasis required involves the regulation of iron entry into the body, regulation of iron entry into cells, storage of iron as ferritin, incorporation into proteins and regulation of iron release from cells for transport to other cells and organs (Lynch 2007).

Nearly all the functional consequences of iron deficiency are strongly related to severity of anaemia, but whether these effects are primarily due to oxygen transport problems or tissue iron deficits is still often unclear. Beard (2001) makes the point that although it is at times convenient to categorize individuals as iron-deficient anaemic vs. iron-deficient non-anaemic, it is actually more logical to consider individuals along a continuum of iron nutriture, with different functional consequences arising at different stages of severity. Nevertheless, in terms of intellectual development, most studies have found that it is not until anaemia is present that an impact is noted, although there appears to be a real continuum in productivity (Kraemer & Zimmermann 2007). With adequate nutrition, a reserve of iron is stored in tissues and is used when insufficient iron is absorbed, such as when dietary intakes are inadequate or bio-availability is low. The size of the body's iron reserve, mostly in the liver, is therefore an index of iron nutritional status. Iron deficiency occurs in three sequential developing stages (Nestel & Davidsson 2002). The first stage is depleted iron stores when the body has no longer any stored iron but haemoglobin remains above the established cut-off levels. A depleted iron store is defined by a low serum ferritin concentration (<12ug/L). Following this is iron-deficient erythropoiesis. As developing red blood cells have the greatest need for iron. at this stage the reduced transport of iron is associated with the development of iron-deficient erythropoiesis. Again the Hb levels remain above the cut-off point but there is an

increase in the transferring receptor concentration and increased free protoporphyrin in red blood cells. The third and most severe form of iron deficiency is iron deficiency anaemia (IDA). This results when iron supply is inadequate for haemoglobin synthesis, resulting in haemoglobin concentrations below the established cutoff levels (Nestel & Davidsson 2002). As noted above, the absorption of non-haem iron is markedly influenced by the iron status. The more iron that is present in the stores, the less iron absorbed (Lynch 2007, Darnton-Hill, Paragas, Cavalli-Sforza 2007). An increased erythropoiesis (e.g. after an acute blood loss) also increases iron absorption.

Stoltzfus (2001b) and others have suggested a new conceptual model citing an evidence-based causality of clinical outcomes. This uses 'tissue iron deficiency' (known to affect work performance and child development), and severe anaemia (known to affect, along with other factors, child mortality, maternal mortality and perinatal mortality). A meeting convened by WHO and INACG in Belmont, Maryland in the US in May 2000, concluded that this was appropriate based on their collective judgment about the strength of causal evidence as in the Table 2.4.

TABLE 2.4: Strength of causal evidence linking iron deficiency or anaemia to health and development outcomes (Stoltzfus 2001b).

A significant body of causal evidence exists for (in order of strength of evidence):

1. iron-deficiency anaemia and work productivity
2. severe anaemia and child mortality
3. severe anaemia and maternal mortality
4. iron-deficiency anaemia and child development

causal evidence is lacking or contradictory for;

- iron-deficiency anaemia and low birth weight, including pre-term birth
- iron-deficiency anaemia and infectious disease, either protective or adverse effects
- mild-moderate anemia and maternal mortality
- mild-moderate anaemia and child mortality

In the regulation of dietary iron uptake, intestinal iron absorption is currently understood to be controlled by three stimuli (Donovan & Andrewes 2004) all of which have potential implications in public health programmes to prevent and control nutritional anaemias. The first is known as “mucosal block” characterized by the inhibition of enterocytes to absorbing iron for several days after a large bolus of iron has been delivered (Hahn et al. 1943 cited in Darnton-Hill, Paragas, Cavalli-Sforza 2007). Mucosal block will most likely occur in systemic iron deficiency because the enterocyte behaves as though it believes that iron requirements have been met. The second stimulus that controls iron balance is the “stores regulator” that can respond to total body iron (Finch 1994). The molecular mechanism has not been clearly elucidated, but it most likely involves saturation of circulating transferrin (Tf). The third regulatory system is the “erythropoietic regulator” that modulates intestinal iron absorption independent of iron body (Finch 1994).

Hepcidin, a new player in the iron trafficking field, appears to play the major role in this mechanism as a recently elucidated systemic iron regulatory peptide, that operates as the key to the mucosal gate (Leong & Lonnerdal 2004, Lynch 2007, Darnton-Hill, Paragas, Cavalli-Sforza 2007). Hepcidin is secreted by the liver and excreted through the kidneys. In experiments in which mice receive a bolus of iron, hepcidin gene expression increases, which suggests that it plays a compensatory response to limit iron absorption (Lynch 2007). Hepcidin is presumed to be a negative regulator of intestinal iron absorption from the diet with its major role as the ultimate regulator of iron homeostasis (Nicholas et al. 2002). It also plays an essential role in regulating iron transport through both placental and intestinal barriers. These same studies on mice identifying the role of hepcidin also exhibited many of the same features of the anaemia of inflammation that is caused by infection, inflammatory disorders, malignancies, and trauma (Roy et al. 2007). Transgenic mice experiments displayed sequestration of iron in macrophages, iron-restricted erythropoiesis and low haemoglobin concentrations, characteristics indistinguishable from the anaemia of inflammation. These important findings have the potential to treat anaemia of inflammation by controlling endogenous hepcidin. In addition, mutations in hepcidin have been documented in humans with haemochromatosis, thus confirming hepcidin’s role as the master regulator of dietary iron uptake. Overall, elucidation of hepcidin’s role has helped shed a new light on the importance of genetics on the process of dietary iron metabolism and its subsequent effect on nutritional anaemia.

The implications of this greater understanding of factors in the control and prevention of nutritional anaemias for public health interventions are still being evaluated but are likely to be important. For example, if populations have high levels of infection, then they will also have high levels of hepcidin, which may then block the uptake of iron that is in the diet from fortification and supplementation (Hurrell & Egli 2007). Hepcidin has not, however, been linked to an effect on dietary haem uptake, thus lending support for promotion of animal-source foods in poor diets (Neumann et al. 2007). Therefore it is becoming more apparent that treatment strategies encompass all the health concerns of a population- nutritional anaemia can only be completely addressed if other diseases are concurrently treated.

2.4.5 Epidemiology

The current estimates of burden

As noted, the figure currently being used is 2,000 million people globally with iron deficiency anaemia (MI/UNICEF 2003), primarily for advocacy purposes. Estimates of global prevalence and burden, inevitably inaccurate anyway, have been further complicated by the frequent misuse of the terms iron-deficiency, iron deficiency anaemia and anaemias generally, sometimes interchangeably and often what is actually being described is unclear (Stoltzfus 2001b). This clearly has implications In terms of assessing progress in the prevention and control of iron deficiency, and in advocacy to policy makers that will be discussed later.

The disability adjusted life years (DALYs) is an expression of years of life lost and years lived with disability and provides an overall estimate of the magnitude of economic losses to a population due to disease (Murray & Lopez 1994). Other indirect social and health consequences of impaired health and vitality are difficult to estimate and are often not considered, although may well be relevant to nutritional anaemias. For example, among resource-poor societies the premature death of a mother and the lower income-generating capacity of iron-deficient and anaemic workers translate into greater rates of disease and overall undernutrition (WHO/UNICEF/UNU 2001).

Anaemia impairs individual growth and development, as well as family, community and national socioeconomic development. The negative impact on national development can be estimated from the number of individuals affected in various age and gender categories; the severity of the deficiency; and the duration and consequences of the condition. The economic implications of such conditions include the costs incurred by the public and private sectors in treating anaemia; the consequences for the society of increased maternal mortality and decreased productivity; and the long-term negative consequences of impaired mental development on human capital formation (WHO/UNICEF/UNU 2001). Based on estimates of iron deficiency anaemia as a risk factor for mortality, when added to the direct sequelae of iron deficiency anaemia, the total attributed global burden amounts to 841,000 deaths and 35,057,000 DALYs (Stoltzfus, Mullany, Black 2004). The authors note the great majority of this disease burden derives from anaemia in pregnancy and early childhood and is borne by women and children, predominantly in Asia and Africa. The economic costs of anaemia due to cognitive delays in children, lower productivity in adults and premature births have been estimated by Ross and Horton (1998), among others and they suggested that the median value of productivity losses due to iron deficiency was about $4 per capita or 0.9% of GDP.

2.4.6 Other causes of nutritional anaemia

Deficiencies of vitamins A, B6, B12, riboflavin and folic acid have all been associated with anaemia, although the pathways are not all clearly established (Nestel & Davidsson 2002, Darnton-Hill, Paragas, Cavalli-Sforza 2007). As well as these specific nutrient deficiencies, general infections and chronic diseases, and blood loss can cause anaemia. HIV/AIDS is becoming an important cause in much of the world, especially Africa. Rarer causes, such as the haemoglobinopathies- inborn genetic errors such as the thalassaemias- also contribute. Malaria, especially when the cause is *Plasmodium falciparum* causes anaemia by rupturing red blood cells and by suppressing the production of new blood cells and contributes up to half of all cases in malaria holoendemic areas in Southern and Eastern Africa (Nestel & Davidsson 2002, Darnton-Hill, Paragas, Cavalli-Sforza 2007). It does not, however, cause iron deficiency as the iron released stays in the body. Helminths, such as hookworms, and flukes such as schistosomes, cause blood and iron loss, as do the nematodes where worm burden is heavy.

In developed countries iron deficiency is the main cause of anaemia. In much of Africa iron deficiency anaemia accounts for about half of the anaemia observed. Where this happens, the demographic composition e.g. anaemia in men, can give an idea of other aetiologies such as malaria (Yip, Stoltzfus, Simmons 1996). Studies in Cote d'Ivoire (Staubli Asobayire et al. 2001) and Benin (Hercberg et al. 1988) showed that about 80% of the anaemic pre-school-aged children had iron deficiency anaemia, compared with 50% of the school-aged children and women, and 20% of the men (Nestel & Davidsson 2002). In a study from Zambia, 62% of the children were anaemic, 3% were severely anaemic and 51% had iron-deficiency anaemia. The authors estimated that if hookworm infection was eradicated, the prevalence of anaemia could be reduced by as much as 25%, iron deficiency by 35%, and severe anaemia by 73% (Stoltzfus et al. 1997). Where the likely contributing cause to anaemia such as helminths and malaria are high, it is important to treat these infections, especially the more vulnerable in the communities. Clearly the success of any intervention depends on whether the intervention deals with the underlying causes (Darnton-Hill, Paragas, Cavalli-Sforza 2007). In many developing countries, it is unlikely that all the anaemia results just from iron deficiency because of heavy loads of intestinal parasites, malaria and other causes of anaemia and so treating just for iron deficient will not have the hoped-for effect. This clearly has significance when assessing the success of goals to eliminate anaemia (as opposed to iron deficiency anaemia) and public health programmes.

2.5 Other micronutrients of current public health significance

The concept of current public health interest is used to justify, in an already very brief background, why micronutrients such as niacin, thiamin, vitamin B12 and selenium are not addressed. Historically, and even now in certain geographic areas, these are, or have been, of important public health interest. Niacin was widespread in many maize-consuming areas, including the south of the USA early last century. It is considerably less often seen these days, not least because of widespread fortification of flour with niacin, amongst other B vitamins and iron (Halstead 1993, Bishai & Nalubola 2002). Thiamin deficiency as beri beri was widespread throughout rice-eating populations (FAO/WHO 2004) and is again less often seen. However, thiamin deficiency's contribution to Wernicke-Korsakoff's syndrome in alcoholics means it is being addressed in a public health manner (in this case fortification of flour) in Australia (Darnton-Hill &

Truswell 1990, NH&MRC 1994). Likewise selenium is being added to the water supply in Finland, although a specific problem has not been identified in humans, although it is likely to be a contributor to Keshan disease near the China/Russia border and countries such as New Zealand have low levels in much of their soil (Thomson 2006). Again, the report of the FAO/WHO meeting in Bangkok in the late 1990s gives useful information on other micronutrients (FAO/WHO 2004). Many of the B vitamins are continuing to be of interest as fortificant pre-mixes being added to flour (both wheat and maize) along with iron and sometimes other fortificants, such as zinc and vitamin A (WHO/FAO 2006, FFI 2005), including more recently in Africa by the Micronutrient Initiative (MI) (FORTAF 2006). Probably the two micronutrients receiving most attention, besides the three already addressed, are folate and zinc.

2.5.1 Zinc

The identification and quantification of zinc deficiency is hindered by the lack of a suitable diagnostic test. Consequently, it has been clearly demonstrated only by intervention trials showing an impact on infectious diseases, more frequently diarrhoea, and less clearly respiratory tract infection. Nevertheless, there is a consensus now that zinc is likely to be a problem in many countries with high child mortality rates (Zinc Investigators' Collaborative Group 1999, Hotz & Brown 2004). It has long been recognized where the deficiency is more florid and has an impact on growth and maturation. It has also been observed as an inborn error of zinc metabolism, acrodermatitis enteropathica, in patients fed incomplete parenteral solutions, in patients with Crohn's disease and occasionally in infants. Failure to thrive, growth retardation, immune effects and delayed sexual maturation are clinical manifestations of zinc deficiency. Zinc-responsive night-blindness has been observed in alcoholism and Crohn's disease (Hallberg, Sandstrom, Aggett 1993).

However from a public health viewpoint, the important aspects have been considered to be the failure to grow and mature successfully, most often found in environments such as the Middle East where the diet is high in phytates and when the diet is marginal and consists largely of unleavened, unrefined bread (FAO/WHO 2004, WHO/FAO 2006). Studies in Jamaican children recovering from malnutrition have shown that zinc status affects not only rate of growth but also composition of synthesized tissue (Golden & Golden 1985). Animal and human studies have shown that vitamin A metabolism and

immune defence and skeletal maturation are especially sensitive to insufficient zinc intake (Hallberg, Sandstrom, Aggett 1993). Supplementation under experimental conditions has shown reduced growth rates and that supplementation was also associated with an increase in energy and protein intake. More recent field trials in Bangladesh, India, Pakistan and sites in Africa have shown conflicting results in growth, reduction in disease, severity of disease and varied results depending on the disease. Nevertheless, results of two recent meta-analyses of such studies seem to indicate a definite role, especially in growth and diarrhoeal disease (Hotz & Brown 2004). Consequently, zinc deficiency and its impact on reducing child mortality has come to the fore, with sufficient evidence that the accepted treatment of diarrhoea is now oral rehydration therapy with a two week course of zinc supplementation (WHO/UNICEF 2004a). There is considerable debate now on whether this also applies to respiratory disease and whether there is a role for the public health prevention of zinc deficiency by supplementation, as opposed to therapeutic use. While it is unlikely that another vertical programme would be instituted there is some pressure to do so.

This is partly due to the difficulty of increasing intakes of zinc through dietary methods, especially poor diets low in animal-source foods (Hambidge & Krebs 2007). Large variations in zinc content can be found between otherwise nutritionally similar food sources but tend to be high in meat, cheese, lentils, and cereals. These tend to be components of more expensive diets. Cereals are the major source of energy and zinc in large parts of the world. As zinc is mainly located in the outer layer of the grain, a low extraction rate means that the majority of the content of zinc, as well as other minerals, are removed, although this should also reduce the phytates that affect bioavailability. Use of zinc-rich galvanized cooking pots and canning may also contribute. Unrefined cereal-based diets present the largest risk for low zinc absorption (Hallberg, Sandstrom, Aggett 1993). Iron content of the diet may also be a factor, as may the presence in the diet of enhancers. Contributing factors may be geophagia and large zinc losses due to intestinal parasitic infections (Hallberg et al 1993). Lower zinc intakes than in western type diets have been described in the fish-based Brazilian diet eaten around the Amazon, and where signs of zinc deficiency were also observed (Shrimpton 1984). Similarly low intakes have been described in other parts of the developing world including South Asia and Papua New Guinea. Nevertheless, Gibson and others have

demonstrated the theoretical possibility and the feasibility in West Africa of increasing the bio-availability of micronutrients in plant-based diets (Hotz & Gibson 2007).

2.5.2 Folate

Folate (or its most common supplemental form of folic acid) has come to prominence recently as the flour in the USA, and other countries, is now fortified with folic acid. Folate is required for DNA synthesis and so its deficiency is clinically expressed in tissues with high rates of cell turnover. The principal sign is megaloblastic anaemia. However, its current public health importance is as a cause of anaemia and neurological tube defects, and possible role in cardiovascular disease. The recent fortification with folic acid in several countries (FFI 2005) was to prevent neural tube defects and success has been demonstrated e.g. in Canada and the USA. There is also some questioning the rationale and continuing debate although it seems clear that neural tube incidence has declined where flour fortification has taken place (Oakley & Mandel 2004). However, there is also a role of lowering homocysteine, which is thought to have an impact on reducing cardiovascular disease (Malinow et al. 1998); and with folic acid's facilitating role it is likely to continue, even if this is a stronger argument in richer countries (Lawrence & Worsley 2007). It has had a longer tradition as a supplement with iron (which will be discussed further in future chapters on effectiveness)). It may also an important cause of anaemia in many places, especially in West Africa (Darnton-Hill, Paragas, Cavalli-Sforza 2007). It was originally described in Bombay (Mumbai) as an anaemia associated with poverty and a diet deficient in animal protein and vegetables (Wills 1993 quoted in Halsted 1993).

2.6 Conclusion

There has recently been considerably more attention given to the fact that quality of diets is a measure of inequity and poverty, and so micronutrient deficiencies rarely occur singly (Huffman & Ramakrishnan 2001, Hambidge & Krebs 2007). This may not be true of iodine in some settings. The relatively recent publication of the FAO and WHO report on vitamin and mineral trace element requirements gives useful overviews of the key micronutrients (WHO/FAO 2006). These details are beyond the scope of this thesis. It is also beyond the scope of this thesis to examine the question of whether affluent populations, often with a majority of the population micronutrient replete, benefit from

more vitamins and minerals (Bendich & Deckelbaum 2001). The next chapter looks at ways in which micronutrients are delivered to be consumed to those that need them, but which often includes the general population, and how coverage, whether by food-based or supplementation strategies, can be increased in deficient populations.

Table 2.5 Country status: VAD public health problem

VAD public health problem[b]	VAD likely public health problem[c]	VAD not a public health problem	No recent data available
Angola	Afghanistan	Armenia	Albania
Antigua and Barbuda	Argentina	Austria	Algeria
Bangladesh	Brazil	Bosnia and Herzegovina	Andorra
Belize	Burkina Faso	Canada	Azerbaijan
Benin	Chad	Cook Islands	Bahamas
Bhutan	China	El Salvador	Bahrain
Bolivia	Congo	France	Barbados
Botswana	Cote d'Ivoire	Germany	Belarus
Cambodia	Ecuador	Greece	Belgium
Cameroon	Georgia	New Zealand	Brunei Darussalam
Cape Verde	India	Palau	Bulgaria
Central African Republic	Indonesia	Poland	Burundi
Colombia	Kazakhstan	Republic of Korea	Chile
Comoros	Mauritania	Russian Federation	Croatia
Costa Rica	Myanmar	Samoa	Cyprus
Cuba	Pakistan	Singapore	Czech Republic
Democratic Republic of the Congo	Papua New Guinea	Spain	Democratic People's Republic of Korea
Djibouti	Saudi Arabia	United Kingdom of Great Britain and Northern Ireland	Denmark
Dominica	Senegal	United States of America	Equatorial Guinea
Dominican Republic	Serbia and Montenegro	Vanuatu	Estonia
Egypt	Solomon Islands	Australia	Fiji
Eritrea	Sudan	Italy	Finland
Ethiopia	Swaziland	Tuvalu	Gabon
Gambia	Tajikistan		Grenada
Ghana	Thailand		Guinea
Guatemala	Turkey		Guinea-Bissau
Guyana	Uzbekistan		Haiti
Honduras	Venezuela		Hungary
Iran (Islamic Republic of)	Viet Nam		Iceland
Iraq	Yemen		Ireland
Jamaica			Israel
Jordan			Japan

Kenya			Kuwait
Kiribati			Kyrgyzstan
Lao People's Democratic Republic			Latvia
Lesotho			Lebanon
Liberia			Libyan Arab Jamahiriya
Madagascar			Lithuania
Malawi			Luxembourg
Malaysia			Malta
Maldives			Monaco
Mali			Nauru
Marshall Islands			Netherlands
Mauritius			Niue
Mexico			Norway
Micronesia (Federated States of)			Paraguay
Mongolia			Portugal
Morocco			Qatar
Mozambique			Republic of Moldova
Namibia			Romania
Nepal			Saint Kitts and Nevis
Nicaragua			Saint Lucia
Niger			San Marino
Nigeria			Sao Tome and Principe
Oman			Seychelles
Panama			Sierra Leone
Peru			Slovakia
Philippines			Slovenia
Rwanda			Suriname
Saint Vincent and the Grenadines			Sweden
Somalia			Switzerland
South Africa			Timor Leste
Sri Lanka			Tonga
Syrian Arab Republic			Trinidad and Tobago
The former Yugoslav Republic of Macedonia			Tunisia
Togo			Turkmenistan
Uganda			Ukraine
United Republic of Tanzania			United Arab Emirates
Zambia			Uruguay
Zimbabwe			
70	**30**	**23**	**69**

[a] Based on clinical and/or biochemical data

[b] Based on *national* data (1989-2004)

[c] Based on *sub-national* data (1989-2004)

Methodology

Criteria for defining countries with vitamin A deficiency as a public health problem:

- Countries: 192 WHO Members States
- Population groups: Pre-SAC, PW
- Data selected from: Last 15 years: 1989-2004 with priority to latest available survey
- Cut-off applied: See table 1

Table 2.6 Prevalence below cut-offs to define a public health problem and its level of importance:

	BIOCHEMICAL		**CLINICAL**		
Degree of severity	**Serum retinol**		**XN**		**X1B**
	PreSAC Serum retinol (<0.70 µmol/L)	**PW Serum retinol (<0.70 µmol/L)**	**PreSAC**	**PW**	**PreSAC**
Mild	≥2-<10%	≥2-<10%	≥1%	≥5%*	≥ 0.5%
Moderate	≥10-<20%	≥10-<20%			
Severe	≥20%	≥20%			

Adapted from: WHO et al. 1996, *UNICEF et a. 1997 and Sommer & Davidson 2002.

- A country has been classified as having "VAD public health problem" when *national data* on clinical and/or biochemical VAD in PreSAC and/or PW has been identified according to classification in table 1. Degree of severity was no taken into consideration for the overall classification.
- A country has been classified as having "VAD likely public health problem" when only *sub-national data (local, district, regional)* on clinical and/or biochemical VAD in PreSAC and/or PW has been identified according to classification in table 1. Degree of severity was no taken into consideration for the overall classification.
- When prevalence data are not reported below cut off, but data on mean SR are available, a country is classified as having a VAD public health problem when the mean SR for the population is <1.05 µmol/L.
- Countries with no data available have not been classified but listed under "no data available".
- National surveys were used over any sub-national data

Chapter Three

The control and prevention of micronutrient malnutrition

3.1 Prevention, control and treatment

As discussed in Chapter One, the recognition of the magnitude of the prevalence and impact of micronutrient deficiencies has resulted in a series of international goals. A meeting in Ottawa in 1991 reviewed and recommended ways to reach these goals (see Chapter 4). These built on experience gained over previous decades (since 1920s in the case of iodized salt). As more experience has been gained (Darnton-Hill et al. 1998a, IOM 1998, MI/UNICEF 2003), and funding increased, these have been continuously refined and expanded. This chapter examines the current most commonly used interventions. Chapter Four then looks at why the prevention and control of micronutrient deficiencies became higher global priorities. Among the reasons suggested is that not only is the problem reasonably easy to demonstrate but interventions are known that can address the problems, and that the impact can be relatively easily measured.

A suggested categorization of such interventions is seen in Table 3.1 (McGuire & Galloway 1994, Darnton-Hill 1998a, IOM 1998, Ahmed & Darnton-Hill 2004) and is broadly:

(i) food-based approaches, including dietary diversification, nutrition education and fortification of staple and value-added foods;

(a) supplementation with vitamin A capsules, iron-folate tablets and iodized oil with increasing interest in a multi-micronutrient supplements and weekly low-dose supplements;

(b) public health interventions such as immunization, adding vitamin A supplementation to other programmes such as National Immunization Days and Child Health Days, promotion of breast-feeding, and treatment of infectious diseases; and,

(c) change in the possibilities that are available to people by modification of the political, socioeconomic and physical environment. As with so much of public health, those most vulnerable to micronutrient malnutrition are those who are poorest.

Table 3.1: Different public health approaches to modifying micronutrient intake used in the prevention and control of micronutrient malnutrition.

Food-based
Dietary diversification
Home gardening
Nutrition education
Development of high micronutrient content varieties of staple foods (also called 'bio-fortification')
Fortification
Staples e.g. flour, noodles
Fats and oils e.g. margarine, edible oils
Condiments e.g. salt, sugar, soy sauce, fish sauce
Complementary foods for infants 6 months and older
Home-based fortification e.g. 'sprinkles'
Beverages e.g. fortified juices, condensed milk and other diary products
Supplementation
National distribution to all preschool children
National Immunization Days
Through health system centers, including MCH programmes, and routine treatment
Outreach e.g. with E.P.I. and other programmes
Post-partum supplementation
'Life Cycle' distribution to adolescents and young women through schools and factories
Home-based supplementation e.g. 'foodlets'
Public health measures
Immunization
Appropriate prevention and control of diseases such as diarrhoea, malaria etc.
Promotion of exclusive breastfeeding
Appropriate complementary feeding
Water and sanitation measures
Appropriate birth spacing
Global equity corrections, poverty reduction and socio-political change
Increased availability and accessibility of micronutrient-rich foods
Improved health systems
Improved status and education of women

The important point about these different approaches is that they are complementary, and should be started in concert, as they may have different time frames and differing

feasibility depending on local circumstances. Behaviour change to improve the intake of micronutrients is an essential part of whatever method is being used; through communications, social and political facilitation, social marketing, and nutrition education. The overall strategy is to reduce the size of the most vulnerable group (to the left of the curve in Figure 3.1) by improving the coverage of the middle group by fortification, dietary diversification and reduction of the disease burden (Darnton-Hill 1998b). The most at-risk group is likely to continue to need supplementation for many years to come (Figure 3.1). The factors listed in Table 3.1 have all been shown, to a greater or lesser degree, to have an evidence-based impact on micronutrient programmes as demonstrated in the following sections.

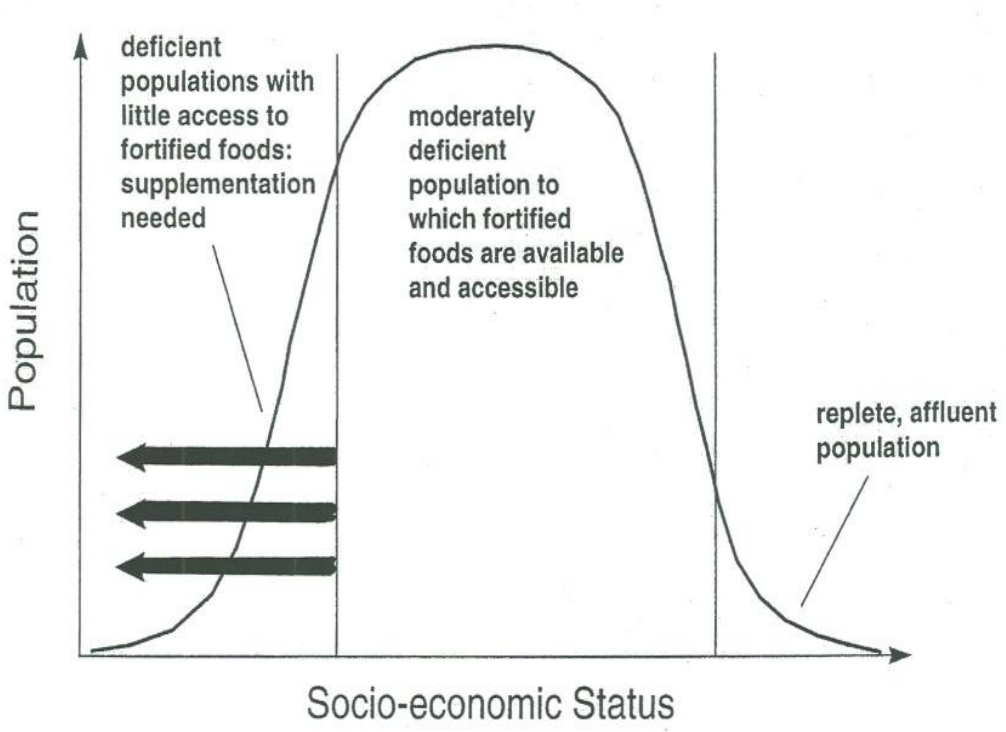


Figure 3.1: Increasing micronutrient intakes in populations, (Darnton-Hill 1998b).

3.2 Food-based approaches and fortification

3.2.1 Dietary and horticultural interventions

With the exception of iodine in certain ecological settings, micronutrients are found abundantly in many plant foods and animal products. However, many poor families do not have enough to eat, as for example in Bangladesh where nearly half of all women are categorized as underweight (HKI 2001a). Of greater significance is the quality of the diet, as diets characterized by poverty are not likely to include many micronutrient-rich foods which are in any case generally more expensive and often less accessible, and so diets are likely to be low in vitamins and minerals, as well as energy (Calloway 1995). This low accessibility to food sources is aggravated by the usually low bio-availability of micronutrients in the diets eaten by poor families and it is poor dietary quality, rather than quantity, that is considered to be the key determinant of impaired micronutrient status (Allen & Ahluwalia 1997).

Food-based approaches have been categorized as: (i) increasing small-scale production of micronutrient-rich foods, by community fruit and vegetable gardening, school gardening and/or small animal, poultry or fish production; (ii) increasing community production of micronutrient-rich foods, such as horticultural products, oil seeds, palm oil, beverages and natural nutrient supplements; (iii) maintaining micronutrient levels in commonly eaten foods with food storage and preservation techniques, improving food safety, and better food preparation; (iv) plant breeding to increase micronutrient levels, including through genetic engineering; and, (v) community strategies to increase consumption of micronutrient-rich foods (Talukder & Bloem 1992, Nemer, Gelband, Jha 2001, Neumann et al. 2007).

In poorer communities where more than 80% of the diet is of plant origin, as in much of Asia and the Pacific, it appears that dietary diversification may be adequate to prevent vitamin A deficiency but not correct it (de Pee et al. 1995, de Pee et al. 1998a). A study of Chinese schoolchildren found they were protected from becoming vitamin A deficient during seasons when pro-vitamin A sources are limited through the consumption of green-yellow vegetables over a 10-week period (but did require about 250g of vegetables per day) (Tang et al. 1999). Nevertheless, studies from Asia and Africa report high prevalences of vitamin A deficiency, even in communities with high intakes of

carotenoid-containing foods (de Pee et al. 1999, Oso et al. 2003). In diets characterized by poverty, iron sources in the diet are especially unlikely to be adequate during pregnancy and in conditions of high parity, and given poor diets and low bioavailability, even in female adolescents before pregnancy. While theoretically it is possible to improve iron status by carefully chosen foods in the diet, it is practically extremely difficult in poor settings (Allen & Ahluwahlia 1997), although Gibson et al. (2000) have demonstrated this for iron, zinc and vitamin A in developing countries. Dietary practices may also contribute to iron deficiency e.g. tea drinking at an early age, even infancy, and to iodine deficiency in the case of goitrogens such as cassava in West Africa. Poor diets are also usually high in phytates, further reducing availability of iron, as well as zinc. Where iron is low in diets, zinc is also likely to be low (Hotz & Brown 2004). Many nutritionists are now identifying the need for animal (including fish) source foods in diets of the poor where they are available and accessible (Allen & Ahluwahlia 1997, HKI 2003a, Neumann et al. 2007, Roos et al. 2007), as well as a variety of strategies to enhance the bio-availability of micronutrients in plant-based diets (Hotz & Gibson 2007).

Nevertheless, improving dietary diversification through increasing variety and frequency of micronutrient-rich food sources through nutrition education and horticultural approaches has been shown to be effective in many settings. Measuring effectiveness should use indicators of outcomes that may go beyond only increased serum levels of micronutrients, to clinical outcomes (reduction in night-blindness) to social outcomes such as women's empowerment (Darnton-Hill et al. 2005a, Bushamuka et al. 2005). Food preparation interventions to achieve dietary diversification can include: nutrition education concerning available foods and their more effective utilization; horticultural approaches such as home gardens; and improved methods of food preparation, preservation and cooking that better conserve the micronutrient content. Inadvertent sources can be important in the diet e.g. iodine in the Australian diet from iodophors used in disinfecting cow teats before commercial milking (Hetzel et al. 2004), and less so, in the case of iron from other sources, such as cooking in iron pots, and less frequently geophagia (Harvey, Dexter, Darnton-Hill 2000). There is also increased interest in the genetic manipulation and breeding of staples and other foods (Bouis, Lineback, Scheeman 2002, Lonnerdal 2003, Darnton-Hill, Margetts, Deckelbaum 2004).

Much of the community nutrition interventions rely on nutrition education, although these are rarely evaluated (Mitra & Darnton-Hill 1988). Nevertheless, interventions in West Africa persuaded fathers to buy liver for their children with presumed improvement of micronutrient intakes (HKI/Manoff research quoted in Darnton-Hill et al. 1998). Devadas (1987) reports several successful behaviour change interventions to increase intakes in India, at least one of which reported a reduction in corneal xerosis (as a manifestation of vitamin A deficiency). HKI (the INGO Helen Keller International) has had documented success in increasing consumption of eggs in Indonesian communities and evaluated the process (de Pee et al. 1998b, de Pee, Bloem, Kiess 2000, HKI 2002). Interestingly, this practice persisted throughout the Asian financial crisis of 1997-98, when it was observed mothers gave up their own weekly consumption to ensure their children continued to consume one or two eggs a week (Bloem & Darnton-Hill 2000). All approaches to preventing and controlling micronutrient deficiencies involve some degree of nutrition education, as some degree of behaviour change is required for all, including fortification.

While *home gardening* is a traditional family food production system widely practised in many developing countries in the world (Talukder & Bloem 1992, Talukder et al. 2000), anecdotal experience suggests home gardening (as an intervention method for improving nutrition) has been generally successful at the pilot or local phase, but often not been scaled up successfully. Recent experience in Bangladesh has demonstrated a successful example where it has (Talukder et al. 2000), and some of the lessons learned are being tried, with apparent good acceptance in Cambodia, Nepal (HKI 2001a,b, HKI 2003a), and parts of Africa such as Ethiopia (Meskel Balcha 2000). An evaluation has shown that food gardening programmes also strengthened the capacity of local NGOs as a contribution towards sustainability of improvements in the community (HKI 2003a,b). So far, the introduction of orange-fleshed sweet potatoes seems to be the most likely successful intervention in Eastern Africa and maybe West Africa (Hagenimana et al. 1999, Ewell & Hagenimana 2000), The additional impact was to tap into women's roles as income-earners and food producers on the one hand, and as food processors and care givers on the other (Hagenimana et al. 1999). Such programmes have a direct impact on vitamin A deficiency, and likely other micronutrients, through increasing the consumption of micronutrient-rich foods, by increasing access through production, preservation and /or distribution between and within households (de Pee,

Bloem, Kiess 2000). They have also been found to increase income and empowerment of women and that can result in increased intake of micronutrient-rich foods such as eggs and meat as well as other foods such as oil, and improved caring practices (Kiess et al. 1998, HKI 2001b, Bushamuka et al. 2005). There appears increasing evidence that some animal sources in the diet are necessary for adequate micronutrient status (Informal Working Group on Feeding of Nonbreastfed Children 2004, HKI 2003a, Neumann et al. 2007, Roos et al. 2007).

Where home gardening is traditionally practised, using such an approach to increase micronutrient intake is more likely to be successful. In Indonesia, ownership of a home garden appears to indicate long-term vitamin A intake from plant foods, which explains its relationship with vitamin A status (de Pee, Bloem, Kiess 2000). In the Bangladesh national survey, young children who had not received a vitamin A supplement, were half as likely to be night-blind if the family had a home garden (Kiess et al. 1998). Home gardens in KwaZulu-Natal showed an increase in dietary intakes, and serum retinol in those with home gardens, but long-term sustainability has not yet been shown in the project (Faber et al. 2000).

Nevertheless there is an on-going scepticism by some public health nutritionists and others and it has been criticized as unrealistic, unsustainable and difficult to scale up (Ruel & Levin 2000, Sommer personal communication 2002). Despite the successful HKI examples, it does seem that a large initial investment needs to be made and then considerable effort in scaling up and monitoring (Talukder et al. 2000) but with potential long term sustainability. It seems likely that in many cases, in order to improve vitamin A intake, and likely iron and zinc, integration of animal sources into the diet are necessary. Because these foods are usually expensive, strategies to include their consumption should include production at the household level by integrating small animal production into home gardening activities. Where this has been done in Asia, programme impacts have included increased egg and chicken liver consumption among poor households (HKI 2003a). Overall, the success of increasing access to micronutrient sources through production, preservation and/or distribution between and within households, as well as increasing income and empowerment appears firmly established (de Pee, Bloem, Kiess 2000).

Many of the conventional cost-effectiveness studies have also, in the opinion of the author, failed to capture some of the beneficial side effects, which, if they could be calculated would give a very much more cost-effective figure- such issues as the demonstrated increase in income to women, increased empowerment and longer term sustainability when successful (Bloem, de Pee, Darnton-Hill 1997, Bushamuka et al. 2005). Because food-based approaches are harder to quantify, involve social change and are less evaluated than say, number of capsules delivered, they have also not received donor support to anything like the same extent as other interventions. This despite the recognized fact that where very low income woman's discretionary income is increased, she is more likely than a husband to use it for food for children, take the children earlier to health systems and even for increasing female education (Quisumbing et al. 2001, Darnton-Hill et al. 2005a,b). Overall, a background paper for the WHO Commission on Macroeconomics and Health, concluded that 'food-based approaches are effective long-term strategies for improving the consumption and production of micronutrient-rich foods but should not replace therapeutic measures, effective in the short-term' (Nemer, Gelband, Jha 2001).

Breeding of high micronutrient-content foods, and genetic manipulation, although currently being promoted as *'bio-fortification'* is very much a food-based approach and will be considered as such. The promotion has recently been most successful, after many years of urging by its proponents, with a very substantial grant from the Gates Foundation and some bilaterals (the Netherlands, USA) to IFPRI (International Food Policy Research Institute) for a project called 'HarvestPlus', to address this emerging possibility (Bouis 2002a, HarvestPlus2005). This is using traditional plant-breeding methods such as identifying plants that have cereal seeds naturally high in zinc or iron, or low in phytates, and then breeding for these. Effectiveness in humans has been shown in one study to date of a successful feeding trial in the Philippines (using nuns to ensure adequate control conditions) (Bouis 2002b, HarvestPlus 2005). The use of genetic engineering is expanding the possibilities, and a relatively recent alliance among IRRI (the International Rice Research Institute) and CIMMYT (the International Maize and Wheat Improvement Center) will increase both efforts and coordination of research efforts on rice, wheat and maize aimed at 'improving the lives of poor farmers' (Bouis 2002b, Lonnerdal 2003, Crop Biotech Update 2005). Poor farmers have not much benefited from transgenic food research up to this point, which has mainly benefited

horticulture for western markets, despite much of the rhetoric (Darnton-Hill, Margetts, Deckelbaum 2004). Probably the best known micronutrient example of this research approach, at least in terms of micronutrients, is the 'golden rice' where four different genes- from the daffodil (*Narcissus pseudonarcissus*) and two from a bacterium (*Erwinia uredovora*) have been introduced to allow a non-biologically active precursor of beta-carotene, to proceed to the next three biological steps to become beta-carotene (Greger 2000, Lonnerdal 2003). It is understood that such bio-fortification will only reach a proportion of the population but if such a variety became accepted by poor farmers, could reach difficult to reach populations (Bouis 2002b, Toenniessen 2002). However, it is not anticipated nutrigenetics will be a significant source of micronutrients in population terms within the next decade (Nestle 2001, Darnton-Hill, Margetts, Deckelbaum 2004).

An interesting recent example has been the identification and revival of high β-carotene containing bananas in Micronesia by Englberger, Darnton-Hill and others (2003). These foods, some of which were traditionally weaning foods, have been identified as containing upto 275 times the amount of β-carotene found in the paler, more commercial varieties like the *Cavendish* as eaten in Australia and other western countries (*Uht en Yap* at 6,110µg β-carotene/100g c.f. 21µg β-carotene/100g). The Pohnpei *Karat* banana, a traditional weaning food in the Federated States of Micronesia contains around 860µg β-carotene/100g (Englberger et al. 2003).

3.2.2 Fortification

Probably the most cost-effective food-based approach to improving nutrient availability and accessibility is fortification, with the proviso that the fortified foods must reach those who most need them. Fortification is defined by the Codex Alimentarius as "the addition of one or more essential nutrients to a food, whether or not it is normally contained in the food, for the purpose of preventing or correcting a demonstrated deficiency of one or more nutrients in the population or specific population groups" (FAO 1996). The fortification vehicle can be either a staple food, or a more processed commercially available food, and many have been tried. The requirements for a potential food vehicle for fortification are well established (Table 3.2) (FAO 1996).

However, not infrequently, those most at risk are outside established market systems that provide many of the 'value-added foods' most likely to be fortified. Nevertheless for

the majority of many populations, fortification of foods with micronutrients has been shown to be a technologically, programmatically and economically effective method of increasing micronutrient intakes in populations (Nestel 1993; Lotfi et al. 1996; Darnton-Hill 1998b). Food fortification is likely to have played a significant role in current nutritional health and well-being of populations in industrialized countries (Bishai & Nalubola 2002). Starting in the 20th century, fortification was used to target specific health conditions: goitre with iodized salt; rickets with vitamin D fortified milk; beriberi, pellagra, and anaemia with B vitamins and iron enriched cereals; and more recently in the USA, risk of pregnancy affected by neural tube defects by adding folic acid to fortified four and cereals. Fortification is now being well supported by donor funds and some Bilateral Agencies such as the Gates Foundation and USAID, to a project called GAIN (Global Alliance for Improved Nutrition) (GAIN 2005). Up to this point, the impact has been limited, especially to poorer populations, but there would appear to be considerable potential.

TABLE 3.2: Requirements for a food vehicle for fortification (FAO 1996)

Commonly consumed by the target population
Constant consumption pattern with a low risk of excess consumption
Good stability during storage
Relatively low cost
Centrally processed with minimal stratification of the fortificant
No interactions between the fortificant and the carrier food
Contained in most meals, with the availability unrelated to socio-economic status
Linked to energy intake

There is now an extensive literature on food fortification programmes, especially recently in the non-industrialized world (Nestel 1993; Lotfi et al. 1996; Micronutrient Initiative 1997; Darnton-Hill 1998b, MI/UNICEF 2004, GAIN 2005, FFI 2005). Fortification of foods is however but one intervention for the prevention and control of micronutrient malnutrition along with other food-based approaches and supplementation; the mix of interventions depending on the local situation, experience, commitment and resources and infrastructure. Fortification has the advantage of requiring relatively less change in consumer behaviors and food habits than the other interventions, although this does not mean that nutrition education and social marketing can be ignored. Without convincing

consumers and policy makers of the need and benefits of fortification, its sustainability will always be at risk (Dary 2001). This has been seen more recently in India, where the Federal Government revoked the mandatory iodization of salt, leaving it to the States, with a predictable decline in iodized salt consumption (ICCIDD 2005). Fortunately, this was reversed but is still be challenged in the Courts (Schultink personal communication 2004).

A relative lack of appropriate centrally-processed food vehicles, less developed commercial markets, and relatively low consumer awareness and demand has meant that over 50 years have passed since its recognized successful impact in industrialized countries (Bishai & Nalubola 2002). However, fortification is now seen as a viable option for the less developed and industrializing countries to increase micronutrient intakes (MI/UNICEF 2003, GAIN 2005). As many of the previous constraints to widespread accessability are minimized and with an increasingly global market, there is a great deal of current interest in fortification as an approach to the prevention and control of micronutrient malnutrition in poorer countries (Dary & Mora 2002, GAIN 2005). The recent fortification guidelines by WHO may also be helping the increased impetus (WHO/FAO 2006). Fortification can, by becoming commercially viable, reduce the size of the at-risk population needing other measures such as supplementation (Figure 3.1). Where the costs are passed onto the consumer, and the food industry routinely fortifies, sustainability is potentially high (Darnton-Hill & Nalubola 2002).

The World Bank has identified micronutrient interventions, in general, and food fortification, in particular, as amongst the most cost-effective of all health interventions and as a major factor in the control of the micronutrient deficiencies in the industrialized world (World Bank 1993). As noted, fortification efforts have in the past been less effective, both in terms of start-up and sustainability, in developing countries compared with the more industrialized world. However, in the last few years, the experience in many countries of Latin America, especially with vitamin A in sugar (Mora et al. 2000, Dary & Mora 2002) and with iron and B vitamins in cereals indicates the potential for considerable expansion of fortification as an approach to address micronutrient malnutrition in the developing world (Murphy 1996, MI 1997, Darnton-Hill & Nalubola 2002, GAIN 2005, MI/UNICEF 2004, WHO/FAO 2006). Iron fortification has been identified as less costly than supplementation but both have been identified as cost-

effective in at least four sub-regions of the world (and that did not even include the predictable impact of interventions on improved intellectual and mental development) (Baltussen, Knai, Sharan 2004). Zambia is now fortifying its sugar with vitamin A (but with unclear sustainability) (Darnton-Hill 1999a), and GAIN has awarded grants to countries such as Cote d'Ivoire, Dominican Republic, Mali, Pakistan and Uzbekistan, as well as China, Morocco and Vietnam (GAIN 2005).

Food fortification programmes that have been successfully implemented in developing countries have been previously reviewed (Lotfi et al. 1996; Nestel 1993; Darnton-Hill 1998; Darnton-Hill & Nalubola 2002, WHO/FAO 2006). The most common food fortification practice has been salt iodization, which has been in existence for over 70 years (Bürgi 1998, Andersson et al. in press). Its success has been largely through its relative simplicity and low cost, but also the international endorsement and advocacy by UNICEF and ICCIDD (International Council for the Control of the Iodine Deficiency Disorders) especially and their coalition of partners. In 1994, UNICEF and WHO recommended universal salt iodization (USI) as the prime approach to correcting iodine deficiency in the many countries where it is a public health problem. In 1992, at the 7th World Salt Symposium in Kyoto, Japan introduced the global elimination goal in a special session presented by ICCIDD Board members. Following this, in 1993 Kiwanis International became an important contributor. Finally, at the 8th Session at The Hague in 2000, the salt industry publicly accepted their specific role and responsibility for delivering the fortified product and the service necessary in achieving and sustaining this goal (ICCIDD 2000, Hetzel et al. 2004, Andersson et al. in press). In 2001, 126 countries in the developing world had salt iodization programs in place (Mason et al. 2001) and new data on this number will be available this year from UNICEF but is expected to be higher.

Iron, folic acid and often other B vitamins were being added to flour or corn staples in 63 countries, and globally 20 percent of wheat flour was fortified in 2005 (FFI 2005), and these figures also continue to increase, building on the early success in the US (Bishai & Nalubola 2002) and later in the Latin American countries (Darnton-Hill et al. 1999a, WHO/FAO 2006). Documentation of the impact of folic acid fortification has been undertaken in Canada, Chile and the USA. While there is surprisingly little hard evidence of impact of iron fortification, circumstantial evidence of the benefit of iron

fortification has been identified in Saudi Arabia, Sweden, Venezuela, and the USA (FFI 2005). CDC (Centers for Disease Control and Prevention in the US) and other partners are currently undertaking surveys that could be helpful in adding to this pool of knowledge in China, Jordan and the United Emirates (FFI 2005). Based on a calculation of 81 countries, it has been calculated the almost nine percent of anaemia cases could be prevented if flour fortification went ahead in all of the countries (Bagriansky on FFI website 2005). There have been trials in Thailand of double fortification of fish sauce, mixed fish sauce and salt brine to address both iodine and iron deficiencies with good efficacy (Chavasit, Nopburabutr, Kongkachuichai 2003). Vitamin A has been less used as a fortificant for mainly technical reasons and cost considerations, but where done has been quite successful e.g. the Philippines has had some success with vitamin A fortification in 'Star' margarine and 13 other food products (Solon et al. 1996, 2000, 2002). There is currently increasing interest in vitamin A fortification of cooking oils and in soup 'bouillon' cubes in West Africa and in oils in Latin America and Africa, and in the spices and flavours sachets in instant noodles in South East Asia (MI 2007).

Following on this extensive increase in fortification programmes over the last couple of decades in developing countries, it is predicted that with increasing urbanization, this trend will continue. The increasing experience with public/private initiatives, on the basis that it is the Food Industry that fortifies foods, not governments, will presumably help this process. However, it is clear that in many low income countries, the public sectors, and foreign aid, are necessary in the early stages (Darnton-Hill & Nalubola 2002). However, it is still not clear how the very poor, with least buying power will have their micronutrient needs met through this approach (Darnton-Hill et al. 2000), and specific targeting and complementary approaches will continue to be needed. Food fortification, supported by clear policies and regulations, has been suggested as likely to play an increasingly large role in the prevention and control of micronutrient malnutrition, but with other interventions needing to be continued to reach the very poor (Darnton-Hill & Nalubola 2002).

A single micronutrient addition to an appropriate food vehicle is increasingly an uncommon approach in food fortification programmes, except iodine in salt and vitamin A in sugar. Even with iodine there is now considerable work in double fortification of salt with iodine and iron (MI/UNICEF 2003, MI 2007) and even triple fortification with vitamin

A as well (Zimmermann et al. 2004b). As Huffman et al. (1998) have described, women in developing countries are often consuming diets of poor bio-availability and limited micronutrient content, leading to concurrent deficiencies of iron, vitamin A, zinc, folic acid, B6, B12 and occasionally other vitamins and minerals. Such deficiencies have important consequences for women's own health, pregnancy outcomes and their breast-fed children's health and nutritional status (Huffman et al. 1998), and increasingly it seems on the birthweights of their children (Fawzi et al. 2007, SCN/WHO/UNICEF 2006). Mason et al. (2001) have estimated that nearly a quarter of children have multiple deficiencies (Mason et al. 2001, MI/UNICEF 2004). Consequently, it is now generally recommended that fortification be with a mixture of micronutrients, often in a pre-prepared fortificant mix of iron, folic acid and other B vitamins (WHO/FAO 2006).

Other facilitating groups may need to be involved e.g. the nongovernmental organizations that have been instrumental in testing the feasibility of small-scale hammer-mill level fortification of maize in Africa e.g. maize meal fortification and hammer-mill technology that was tested for effectiveness in Zimbabwe. Families bring their maize to the hammer mill and are offered a sachet of premix (vitamins A, B group, iron and zinc) costing approximately $US0.80 to add to 20 Kg of maize meal. Evaluated after 1 year, half of all maize in the operational research area was being fortified (although the local mixing process was seen as taking too long and a constraint) (Lindsey & Kwaramba 2001). Similar pilots have also been taking place in Malawi, Mozambique, Tanzania and Zambia. Quality assurance and quality control have been identified as challenging issues under these circumstances. Mobile self-contained mills for fortifying maize in refugee camps are also being tried. The UN World Food Programme (WFP) is involved in Afghanistan and Bangladesh; the WFP is facilitating locally fortification of WFP flour with vitamins A, B1, B2, niacin, folic acid, and iron. Issues of scaling-up and sustainability will also still need to be overcome in these efforts.

Even though fortified foods may not reach the distant rural and poorer populations, this may be becoming increasingly less true in many countries; it is predicted that half the global population will be urbanized during this year (2007). Where isolation, both geographically and societally exists, other measures are then needed for these unreached populations, such as other food-based approaches and supplementation. The need to complement supplementation e.g. by fortification, is however important as

supplementation may not reach non-pregnant women, female adolescents and young children, who are not usually being directly targeted by supplementation programmes which are almost universally targeted to children 6 months to 6 years, post-partum women and in antenatal care (WHO/MI 1998, WHO 2001). Other groups, all of whom have been shown to be vulnerable to micronutrient deficiencies, especially pre-pregnant women (Huffman et al. 1998, Bloem, de Pee, Darnton-Hill 1998, Christian 2003) might well be reached by appropriately fortified foods. One concern is infants and young children who usually do not eat sufficient enough fortified foods to have their vitamin and mineral requirements reached. Then they need commercially available fortified complementary foods or special programmes. One example is the *VitaLeite* programme in the State of Sao Paulo in Brazil where the distribution of free milk, fortified with vitamins A and D and iron, is targeted to over 700,000 poor families. A small survey (n=269 children 6m-2y) in Angatuba found anaemia prevalence dropped from 62.3% to 26.4% in one year (Ferrer 2001). In Asia, at least, investment per head in fortifying staples and complementary foods for older infants is one tenth that of supplementation programmes (Mason et al. 1999). Fortification of local complementary foods has been shown not only to improve young child status, but where the community is involved, to empower the women in these communities. Another important delivery mechanism using fortification is the internationally-recognized imperative of fortifying all food used in humanitarian aid, although this is tragically occasionally still not done, although increasingly less so, as it is an underlying pre-requisite for WFP (U.N. World Food Programme) (Webb 2003).

Exactly what is meant by fortification and what constitutes a fortified food has expanded. These now include: a single micronutrient added to food, multiple micronutrients added to foods (e.g., triple fortification of salt), supplement-type home fortification (e.g. 'sprinkles'- tasteless multimicronutrient additives) added to weaning foods and, foods bred or bio-engineered to contain micronutrients that are not present in the traditional varieties ('bio-fortification'), and vastly improved fortification techniques, allowing for multiple, stable, and acceptable fortification. 'Sprinkles', are microencapsulated micronutrients, including ferrous fumarate, which are available in a single dose sachet, and can be sprinkled onto complementary and weaning foods and other foods. In a randomized, controlled trial in Ghana, they were found to be as efficacious as iron drops in the treatment of anaemia (Zlotkin 2001). There is extensive experience with efficacy

studies such as those carried out in Bangladesh, Benin, Bolivia, Canadian First Nations and Inuit areas, China, Haiti, India, Nicaragua, Pakistan, Sri Lanka and Vietnam (Supplefer 2005). Although there was initially some concern about the levels of iron being given, these have now been reduced and there seems no doubt about their efficacy. Cure rates from anaemia have ranged from 55-90% in children in the studies conducted (Supplefer 2005, Zlotkin & Tondeur 2007). In another public/private enterprise, the Heinz Company promoted 'Sprinkles' free of cost during the current Tsunami crisis in South Asia, and will do so in other appropriate circumstances. So, while the effectiveness applications need further demonstration, considerable experience has been gained in the post-Tsunami disaster areas in South Asia (de Pee et al. 2007) and non-emergency settings (Zlotkin & Tondeur 2007).

While multiple fortification has long been used in flour and breakfast cereals (Bishai & Nalubola 2002, WHO/FAO 2006), many micronutrients are now being added to other commercially processed foods, including confectionery foods in Indonesia (Sari et al. 2001), lozenges in Bangladesh and India (Laviolette et al. 2004); fortified drinks in Nicaragua, Peru, the Philippines and Tanzania (Micronutrient Initiative 1997; Solon 2001, Ash et al. 2001), and a short-bread type biscuit in South Africa (van Stuijvenberg et al. 1997). The efficacy of fortifying fish sauce with 10mg iron as NaFeEDTA in 10 ml of fish sauce has been demonstrated in Vietnam (Thuy 2001, GAIN 2006) and iron fortification of soy sauce trials are well underway in China (Fidler et al. 2001) and preliminary results are most encouraging (GAIN 2006) with clear reductions in anaemia prevalence. The fortificant used is unfortunately relatively expensive and would have to be passed onto the consumer at some point if sustainability is to be assured.

What is the future for fortification? It has considerable funding support, there is a clearly identified need for interventions to combat micronutrient deficiencies worldwide, and there is considerable experience in industrialized countries and its spread will be helped by the current globalization processes. In the more affluent industrialized countries, micronutrient deficiencies have been, and continue to be, addressed by food fortification, as well as by overall economic growth and general improvements in health, sanitation and nutrition that have contributed to the prevention and control of these deficiencies. These same aspects must be addressed in any prevention and control programmes in non-industrialized countries. Fortification, supplementation, other food-based

approaches, and complementary public health measures are all necessary. This will only be done by partnerships with government, industry, and the consumer. There is a need to assess more widely the impact of interventions, not least for advocacy. Ultimately the success, impact, and sustainability of food fortification, like other interventions, rest with educating the consumer, developing consumer demand and demonstrating impact.

3.3 Supplementation

Supplementation has often been characterized as a short-term approach, criticized as an example of medicalization of a public health intervention, and presumed to have difficulty with likely sustainability, especially when supplements are supplied by foreign donors. Nevertheless, iron supplementation, and for many years now, iron with folic acid, has been the method of choice to address anaemia in pregnant women. This is despite, limited evidence of its effectiveness and limited impact (Viteri 1997, Mason et al. 2004, Darnton-Hill, Paragas, Cavalli-Sforza 2007), although efficacy has been repeatedly shown in smaller studies (Schultink et al. 1997, Nestel & Davidsson 2002, MOST 2004). Vitamin A supplementation has now been in place for over 30 years in countries such as Bangladesh and so hardly merits being seen as short-term, and many would argue that the need will be there for many years yet (Sommer & Davidson 2002, Sommer et al. 2002, West & Darnton-Hill 2007). Zinc supplementation is now seen as the recommended treatment for diarrhoea in children in developing countries (WHO/UNICEF 2004b), and while not used, at least as yet, in prevention, probably reduces the risk of recurrent attacks of diarrhoea for some months after treatment (Sazawal et al. 1995, Shrimpton et al. 2002). The impact of iodine supplementation was first demonstrated in Papua New Guinea in pregnant women as an intramuscular injection, and an oral supplement is increasingly being recognized as necessary for short-term needs, and emergencies, and perhaps in most pregnancies (Hetzel & Pandav 1997, de Benoist et al. 2007, Untoro et al. 2007). Multiple micronutrients are regularly consumed by a majority of the adult population in several affluent countries, and are recommended in pregnancy in the USA and in the elderly. Their use in the Developing World has been slower to take on, as they are being more rigorously evaluated than they ever were in the industrialized world (Åke Persson, Eneroth, Ekstrom 2004, Tomkins 2004). Nevertheless, their widespread use and endorsement in a series of WHO and WHO/UNICEF recommendations are ensuring this remains a major approach to the

prevention and control of micronutrient deficiency, and several expert consultations on their use as a public health intervention are likely moving their adoption ahead in developing countries UNICEF/UNU/WHO 2004, Fawzi et al. 2007, SCN/WHO/UNICEF 2006).

The Canadian Government for example is a major donor to UNICEF (through the Canadian INGO The Micronutrient Initiative) of vitamin A supplements. As was seen in the previous chapter, the rationale of supplementation with high doses of vitamin A (usually as retinyl palmitate) rests on the fact that this fat-soluble nutrient can be stored in the body, principally in the liver. Periodic high-dose supplementation (200,000IU or ~6,600mg every 4-6 months) is thus intended to protect against vitamin A deficiency and its consequences by building up a reserve of the vitamin for periods of reduced dietary intake or increased needs (Sommer & West 1996, WHO/UNICEF/ IVACG1997, IOM 1998, Bloem, de Pee, Darnton-Hill 1998, de Benoist, Martines, Goodman 2001). National coverage to all preschool children with vitamin A capsules has in the past been hard to sustain over time and may not reach the children most at-risk (Darnton-Hill et al. 1988, Reddy 1989, Bloem, de Pee, Darnton-Hill 1998), although using National Immunization Days was a successful recent experience (UNICEF 1998b). Other approaches are now being used to complement current methods of reaching the most at-risk groups- generally children under five and women of reproductive age (Dalmiya, Palmer, Darnton-Hill 2006). Opportunistic supplementation, by more medically targeting sick children when they present to Health Centres with measles, malnutrition, or infectious diseases such as diarrhoea, has had widespread adoption, at least in policy although coverage remains low in many countries.

Another emerging approach is the use of Child Health Days and is showing unexpected promise (Dalmiya et al. 2007) in child survival and development programmes when given with other interventions such as deworming and insecticide-treated bednets. A recent article approaching the integration from the helminth control side notes that while treating neglected worm diseases is an essential first step to improved health, antihelminthic drugs need to be integrated with simple and inexpensive nutritional interventions such as micronutrient supplements, both to promote recovery and to strengthen impact (Hall 2007). The guidelines for supplementation for infants and children are being revised by WHO with UNICEF and the Micronutrient Forum. IVACG

earlier suggested modifications that include doses to infants less than six months and increasing the postpartum dose by a further 200,000IU 24 hours after the first one (Sommer & Davidson 2002), but that have not been endorsed by WHO and so not widely implemented. Still, the increasing consensus is that many national situations require immediate national vitamin A supplementation programmes and that these will last into the foreseeable future, unless the local and global inequities are greatly reduced (Sommer et al. 2002, Ramakrishnan & Darnton-Hill 2002).

Because of the recognized efficacy and effectiveness of vitamin A in deficient populations (Sommer & West 1996, Bloem, de Pee, Darnton-Hill 1998, West & Darnton-Hill 2001, Dalmiya, Palmer, Darnton-Hill 2006), supplementation has been re-emphasized as the prime intervention several times since a consensus statement of International Agencies, some bilateral agencies and an International NGO (Helen Keller International) (IVACG/UNICEF with MI/WHO/CIDA/USAID 1997). With coverage in National Immunization Days (NIDs) that regularly reached over 85-90% this re-affirmation was appropriate (UNICEF 1998b) but had some time limits, as the polio NIDs are phased out (which may however be continued for longer than originally thought in West Africa and South Asia because of small but worrying resurgences of poliomyelitis cases in India and Nigeria). The challenge has been to translate this into micronutrient days, preschooler health days, Child Health Days vitamin A days etc., two times a year as the polio NIDs are discontinued. There is already experience of success in countries as diverse as Niger and the Philippines. A previous USAID Micronutrients Project reviewed seven successful country examples (MOST 2004), and UNICEF has more recently reviewed progress (Dalmiya, Palmer, Darnton-Hill 2006, UNICEF 2007b). More than two thirds of children in the least developed countries received at least one vitamin A supplement in 2002 (Dalmiya, Palmer, Darnton-Hill 2006, UNICEF in press). While it is recognized this will not adequately protect a child, more than 13 countries are now achieving over 70% coverage twice a year- the minimum coverage needed (UNICEF 2007b). And more emphasis is being paid to the required minimum of two doses and will be reported upon later this year (2007) in a report on the progress towards the UN World Fit for Children goals but has already shown progress in increased numbers of countries (UNICEF 2007b, Dalmiya, Palmer, Darnton-Hill 2006).

A strategy in line with an increasing emphasis on a 'life-cycle' approach to preventing vitamin A deficiency, is to give a capsule to a mother immediately post-partum and strongly encouraging breast-feeding (Bloem, de Pee, Darnton-Hill 1998, de Benoist, Martines, Goodman 2001, Sommer & Davidson 2004). The poor diets that women in developing countries are often consuming due to poor availability and limited consumption of micronutrient rich foods, leads to deficiencies of vitamin A and other vitamins and minerals. Such deficiencies have important consequences for women's own health, pregnancy outcomes and their breast-fed children's health and nutritional status (Huffman et al. 1998, SCN/WHO/UNICEF 2006). WHO presently recommends that women in high-risk populations be given 200,000 IU of vitamin A within 6-8 weeks postpartum as a means to improve maternal status, raise breast milk vitamin A concentrations and improve liver stores of breast fed infants (WHO 1997). Studies in Bangladesh, however, found this dosage to maintain adequate maternal serum and breast milk retinol levels for only the first 3 months postpartum (Rice 1999), and similarly in Kenya (Ettyang et al. 2004), raising concerns about the adequacy of this regimen in achieving a sustained improvement of vitamin A status of lactating women. Further concerns have been raised by recent research reports for the ZVITAMBO trials in Zimbabwe (Humphrey et al. 2006) in relation to women in highly endemic HIV populations. The current recommendations for safe dosages to women are available from WHO (WHO/UNICEF/IVACG 1997) but these do not address HIV issues, which are unresolved. It seems vitamin A supplementation to women will not reduce transmission but may have other positive impacts on birth outcomes and the infants health (Friis 2006). This is also supported by research in Tanzania by Fawzi et al (2004a,b) and Friis et al. (2004) in east African populations. Further research is urgently needed in this area, and is on-going in several countries. This issue was addressed in an Expert Consultation. at the UNICEF Innocenti Centre in Florence in April 2005 without resolution.

Delivering multiple micronutrients, including vitamin A, using existing delivery systems such as those for iron/folic acid tablets for pregnant women, is also currently being actively explored (UNICEF/WHO/UNU 1999, UNICEF/UNU/WHO 2004, SCN/WHO/UNICEF 2006). In line with the above-mentioned 'life cycle 'approach, there is similarly already some discussion on multimicronutrient powders for children, and using other delivery systems (e.g. boarding schools, factories etc.) for younger women of

child-bearing age. Examples include HKI's experience in Indonesia (Bloem personal communication), including multimicronutrient supplementation such as the 'Foodlet' which has mainly been investigated with children (Gross, Dwivedi, Solomons 2003, Shrimpton & Allen 2005) and multiple micronutrients in the micro-encapsulated 'Sprinkles' form (Zlotkin & Tondeur 2007). The 'foodlet' is a chewable, water-dispersible flavoured supplement which is also crushable and is suggested for use as a home-fortificant as well as a supplement (Gross, de Romana, Tomaro 2000). It contains one RDA (Recommended Daily Allowances) of each of 13 micronutrients (except iron which is a half RDA) and research has confirmed its efficacy but effectiveness remains to be established (Shrimpton & Allen 2005). There is the UNICEF (UNICEF/WHO/UNU 1999) formulation of a multimicronutrient supplement for women of child-bearing age, which has been extensively tested for both efficacy and effectiveness. An early assessment shows effectiveness in raising micronutrient status, but also in raising birthweight by on average 67g which while likely to be clinically significant was not statistically so (Åke Persson, Emeroth, Ekström 2004). However, a subsequent meta-analysis of 12 datasets showed a small but consistent and statistically positive effect on mean birthweight of nearly 25g, despite the trials being conducted in a large variety of different environments e.g. delivery systems, maternal micronutrient baseline status, very different maternal weights and heights and so on (SCN/WHO/UNICEF 2006). A decision on WHO/UNICEF recommendations on the use of multimicronutrient supplementation will be made on the basis of further evidence and expert consultations in the next few years, as it has proven surprisingly controversial.

Iron and folic acid supplementation has been the traditional approach to addressing iron deficiency, particularly during pregnancy (DeMaeyer et al 1989, Stoltzfus & Dreyfuss 1998, WHO 2001) but logistics are an issue as it is relatively expensive and coverage is often poor. Poor compliance is usually blamed but at least two reviews of the topic have indicated that distribution and logistical problems were every bit as important (Gillespie, Kevany, Mason 1991, Galloway & McGuire 1994, Galloway et al. 2002). Interesting work is proceeding in a number of centres examining the efficacy of intermittent dosages, once or twice a week, suggesting that this may be a possibility for prevention, although not to treat anaemia in pregnancy (UNICEF/UNU/WHO/MI 1998). However it does appear appropriate to recommend a dosage regimen of one or two times per week before pregnancy e.g. to adolescents and young women in schools and

factories (Gross et al. 1997, MOST 2004). It is presumed this approach would encourage compliance and reduce side effects and would certainly reduce costs (Schultink et al. 1995, Viteri 1997, Cavalli-Sforza et al. 2005) but not logistic requirements, a recognized constraint in many settings. Work in four Asian countries has shown promise with a social marketing approach (Cavalli-Sforza et al. 2005). With iron supplementation, gains in productivity and take-home pay have been shown to increase 10-30% (WHO 2001). Consequently there are important reasons, in addition to the already compelling health, cognitive development and reproduction consequences, to accelerate programmes to prevent and control iron deficiency anaemia (UNICEF/UNU/WHO/MI 1998, WHO/UNICEF 2004).

Nevertheless, there is increasing consensus that new approaches are required (UNICEF/WHO 1995, UNICEF/UNU/WHO/MI 1998, LINKAGES 2001, Nestel & Davidsson 2002, Molyneux & Nantulya 2004, Darnton-Hill, Paragas, Cavalli-Sforza 2007). Antihelminthic treatment improved the haemoglobin and serum ferritin concentrations of Tanzanian schoolchildren (Bhargava et al. 2003), growth, appetite and anaemia (Stoltzfus et al. 2004a) with similar positive synergies in other settings (Hall 2007). As the strategy for improving micronutrient status moves more towards integrated approaches as a way of helping to improving child survival (Bryce et al 2003, Dalmiya 2007), reducing micronutrient deficiencies will be increasingly seen as an approach to increasing child survival and development.

Programmatically shorter-term approaches for iodine have included iodized oil injections which were spectacularly successful in the highlands of Papua New Guinea (Hetzel & Pandav 1997) but the programme appears not to have been sustained. Although there are the constraints of injections and sterility, cost, diversion of effort from salt iodization and sustainability, there would still seem to be a limited role for hard-to-reach, unsophisticated populations and in emergencies. The effect appears to last for three years at least. Cheaper and programmatically more feasible but effective for only a year, is iodized oil taken orally (WHO 1996b, Hetzel et al. 2004, Untoro et al. 2007). Supplementation with oral iodized oil (or intramuscularly) has not been extensively expanded, even in areas where iodized salt is not reaching, or where it is unlikely to reach, such as in acute emergencies. This was largely because a policy decision was made by UNICEF in 1995 whereby all efforts, and funding, would go into the universal

iodization of salt (USI). This has been spectacularly successful, increasing access by households to iodized salt from <20% in the early 1990s to almost 70% in 2000 (Dalmiya & et al. 2004). However, there are now concerns that this has plateaued and so UNICEF and other partners developed an acceleration strategy to try and reach the last 30% in time for the UNICEF goal at the end of 2005 (Mangasaryan 2007). The Network for the Sustainable Elimination of Salt is also developing one that will include the UNICEF strategy and other partners such as ICCIDD and the Salt Producers, to achieve the same goal but oriented towards sustainable elimination subsequent to achieving universal salt iodization (USI). However the Network has been of limited effectiveness up to this point. Part of this strategy includes a gap analysis (developed by the author and co-workers, to identify gaps in national programmes and then to address these and which will be discussed further in the monitoring and evaluation section (chapter 5). Part of this is because there is an understanding that the 'low-hanging fruit' have been plucked and that the remaining communities to be reached will need more than one approach. There is also the human rights aspect where populations, e.g. in emergency situations and refugee camps cannot wait until iodized salt becomes available. While the universal iodization of salt will remain the overwhelmingly more important intervention, supplementation with iodine is likely to become an increasing part of the overall strategy for the remaining unreached groups.

3.3.1 Multiple micronutrients

As noted above, and as Huffman et al. (1998) and others (Mason et al. 2004, Neumann 2007) have shown, women in developing countries are often consuming diets of poor bio-availability and limited micronutrient content, leading to concurrent deficiencies of iron, vitamin A, zinc, folic acid, B6, B12 and occasionally other vitamins and minerals. Children in poor countries, and even in disadvantaged children in more affluent countries, are also frequently suffering from more than one micronutrient deficiency (Gross, de Romana, Tomaro 2000, Mason et al 2001). Mason et al. (2001) have estimated that nearly a quarter of children have multiple deficiencies (Mason et al. 2001, MI/UNICEF 2003). UNICEF has provisionally recommended that a combined vitamin-mineral supplement for pregnant women, similar in composition to those freely available in the more industrialized world, is an option that needs to be considered for developing countries (UNICEF/WHO/UNU 1999). As also noted above, considerable research has been going on looking at various outcomes such as incidence of low birth weight,

maternal haemoglobin, and perinatal mortality (UNICEF/UNU/WHO 2004), progression to AIDS in women with HIV (Fawzi et al. 2004, Tomkins 2004), morbidity and micronutrient status in children (Gross, Dwivedi, Solomons 2002) and both efficacy and effectiveness of intervention trials (SCN/WHO/UNICEF 2006).

Various intervention strategies are also being tested, with positive results emerging for such strategies as 'sprinkles', 'foodlets' and multimicronutrient supplementation, alongside on-going efforts to scale-up fortification and other food-based approaches. Effectiveness trials of the 'foodlets'- the IRIS trials in four countries- found limited impact on morbidity but increased micronutrient levels and reduced anaemia (Gross et al. 2005). An important underpinning of this approach is the 'life-cycle' concept, whereby the micronutrient status of the adolescent girl, is recognized to affect her status when she goes into pregnancy, which then affects the foetus and neonate in a variety of ways, including low breastmilk levels of some micronutrients such as iron and vitamin A. Multimicronutrient powders such as 'Sprinkles' seem therefore likely to become increasingly important programmatically (Zlotkin & Tondeur 2007) especially in emergencies (de Pee et al. 2007). A WHO/WFP/UNICEF statement recommending this has recently been published.

3.4 Treatment

The distinction between prevention, control and treatment is often blurred in micronutrient programmes, except in serious deficiency e.g. xerophthalmia, anaemia <7g/dl. Children with any stage of xerophthalmia should be treated with vitamin A according to WHO treatment guidelines; i.e. with high potency vitamin A at presentation, the next day and 1 to 4 weeks later (WHO 1992). Supportive nutritional and antibiotic therapy should be considered, as indicated by the patient's condition. Early childhood night blindness responds within 24-48 hours to high-potency vitamin A treatment. However, the efficacy of the WHO guidelines to treat pregnant nightblind women with either 25,000 IU each week or 10,000 IU daily for at least 4 weeks is only presumptive (WHO/MI 1998). A randomized trial in Nepal recently reported that long-term, weekly supplementation with ~23,000 IU only prevented about two-thirds of maternal night blindness cases (Christian 2003) suggesting that a higher, more frequent or sustained dosage may be needed to achieve optimal efficacy. This is now being questioned yet

again, especially in populations with high prevalences of HIV infection, where, there is some suggestion that vitamin and iron supplementation in replete populations may actually encourage the virus to replicate (Fawzi et al. 2004b, Humphrey et al. 2006). On the other hand there is now increasingly encouraging results suggesting that multimicronutrients may help delay progression of the disease (Fawzi et al. 2004a, Friis et al. 2004).

As there are standard guidances for treatment of micronutrient deficiencies, and these are usually well tried and efficacious, they will not be discussed further. WHO is the technical agency of the United Nations system that takes a normative role in developing these on an evidence-base and consensus of experts (www.who.org). The prevention of micronutrient deficiencies, although undoubtedly efficacious remains challenging in terms of effectiveness, especially in hard-to-reach populations. Recent research in Pemba in Zanzibar, Tanzania has raised again the question of the safety of iron supplementation to children with adequate stores and especially in malaria endemic areas (Sazawal et al. 2004) but the need to treat anaemia has recently been reinforced by guidance from WHO/UNICEF (2004a). Similarly, vitamin A treatment and prevention in HIV endemic populations is being questioned, along with iron and zinc but supplementation with a multimicronutrient supplement of one 1 RDA, (except iron which is half an RDA) continues to be recommended, and much current work is being devoted to extending guidance. With iodine, the concern is more whether women at risk, especially pregnant women, will get enough for both treatment and prevention, without supplementation. WHO/UNICEF have issued a guidance note on the treatment of diarrhoea and for the first time explicitly recommend 2 weeks treatment with 20g (2RDAs) of zinc (WHO/UNICEF 2004b).

All of the current on-going programmatic research in the area of multiple micronutrient supplementation is only briefly touched upon here, but will be a major area over the coming years. As noted, several technical consultations were held in 2005 and 2006 to clarify results and to inform UNICEF guidance to its Country Offices on both treatment (e.g. the recent joint WHO/UNICEF guidance on the use of zinc in the treatment of diarrhoea) but more importantly, given the nature of public health, on prevention and control.

3.5 Related public health interventions

For maximum impact other public health interventions are essential. These include control of infectious diseases, expansion of measles and other childhood immunization interventions, deworming for intestinal parasites (hookworms), malaria control, promotion of breast-feeding, and proper health care such as oral rehydration therapy, all of which have an impact on micronutrient status (Gillespie & Mason 1994, The Bellagio Child Survival Study Group 2003, Dalmiya, Palmer, Darnton-Hill 2006, Hall 2007). Breastfeeding is identified in the Bellagio child survival reports as the most important intervention with around 13% of impact (Black, Bryce, Morris 2003). However, the issue of HIV-infected mothers, and the possibility of insufficient vitamin A (Ettyang et al. 2004, Grubesic 2004) and iron, especially in premature neonates, will need continued work on the best guidance in this minority of cases. Vitamin A and iron supplementation of pregnant Indonesian women benefitted the vitamin A status of their infants, but the authors concluded in that study that the infants may need vitamin A supplementation or increased dietary intake after six months (Schmidt et al. 2001).

Among the major remaining constraints, as the recent re-analysis of the Child Survival approach has reminded the international health community, are poor health systems and inadequate resources (Black, Morris, Bryce 2003, Bryce et al. 2003). They also demonstrate convincingly that it is not that cost-effective interventions are not known, but that they are not being implemented on a sufficient scale (Bryce et al. 2003, The Bellagio Study Group on Child Survival 2003). This will be further examined in Chapter 6. Largely based on this series but including areas of traditional involvement, UNICEF altered its priorities for its next five year programme of operations (the Medium Term Strategic Plan 2006-2009) which has as its results areas the reduction of: the diseases of childhood, reduction of the vaccine-preventable diseases, neonatal causes of death, undernutrition, water and sanitation-related disease and strengthening of national policy to support health systems and coordinate funding through the various political and policy mechanisms such as the PRSPs (Poverty Reduction Strategic Plans). With relation to the topic of this thesis, the consensus of the Group explicitly recognized the importance of vitamin A, iron and zinc in increasing child survival (Black, Morris, Bryce 2003).

With the recognized interaction between infectious disease and undernutrition, addressing just malnutrition or just disease control in isolation is unlikely to be

successful. Infectious disease can have an effect on micronutrient intake, absorption and utilization. Vitamin A deficiency and iron deficiency anaemia can affect immune status and vitamin A deficiency is now well accepted to be associated with something like a 25% increased likelihood of child death, especially from the diarrhoeal diseases and measles (Beaton et al. 1993, Sommer & West 1996). Because of the coexistence of multiple micronutrient deficiencies and interactions between micronutrients, and because micronutrients are generally ingested as part of the daily diet, it appears logical to pursue an integrated approach covering more than one micronutrient. For example, treating iron deficiency anaemia with both iron and vitamin A has a greater effect than either of the two micronutrients alone (Suharno et al 1993, Bloem et al. 1990). Iron-zinc supplementation in Indonesian children impacted on iron and zinc status but also vitamin A status (Schultink et al. 1997). In IDD- and VAD-affected children receiving iodized salt and concurrent vitamin A, supplementation improves iodine efficacy (Zimmerman et al. 2004a). This clearly has important programmatic and policy implications.

There are, however, arguments both for and against such integrated approaches. It should be more convenient and cost effective to target the same populations for all three micronutrients using the same health or social infrastructure and the same workers e.g. as in the VADAG approach in the Philippines and VAC in Vietnam (Darnton-Hill 1998c), and as earlier strongly advocated by Underwood as part of the (IS) Institute of Medicine document on micronutrienrs (IOM 1998). Mitigating against this approach is that the age range of the targeted groups are somewhat different; vitamin A deficiency being most common in the second and third years of life, iodine deficiency most critical in women of reproductive age, and iron deficiency anaemia being found most commonly in the first 1-2 years of life and in pregnancy. Nevertheless women and children, and especially those in poverty, are predominantly those most at risk for all three micronutrients, and it is this equity argument that is currently driving the debate (Victora et al. 2003).

Such discussions have gone backwards and forwards over the last two decades. There is no doubt that vertical micronutrient programmes have been successful, at least for vitamin A and iodine, especially in implementation, and presumably impact, although this has not been conclusively demonstrated as yet (and there seems little appetite on the part of donors to fund such impact studies). Nevertheless with discussions such as those sparked by the Bellagio Group findings, it is clear there will be a return to a more

integrated approach, especially with the cessation of the national immunization days, and the increasing number of interventions and 'lobby' groups demanding attention e.g. IZiNCG, FFI, GAIN, GAVI, PMNCH and so on. In most affected countries, the resources (especially human but also the health system) cannot support so many vertical programmes without distortions. GAIN and GAVI have been cited as examples of this (Richter 2003).

Nevertheless, based on increasing experience with IMCI (Schellenberg et al. 2004, El-Arifeen et al. 2004), Nutrition packages (LINKAGES 2005) and outreach like Child Health Weeks (Aguayo et al. 2004), and on the established evidence base of the Bellagio Study Group Child Survival papers (2003), it is clear that integrated approaches are being increasingly adopted. The emphasis in this is likely to be on integrated approaches to reducing child mortality, and programmes for the prevention and control of vitamin and mineral deficiencies will therefore be seen as to how they contribute to this goal (especially the Millennium Development goal number 4- see Chapter 4), and will be integrated with other interventions. The goal will then become how to do this most effectively, and will be discussed more in chapter 6.

Micronutrient deficiencies prevention and control will remain an important part of overall public health approaches in resource-poor settings. Noting that potential investments appear under-resourced, Behrman and colleagues have also demonstrated the high benefit-to-cost ratios and noted that the 'gains appear to be particularly large for reducing micronutrient deficiencies in populations in which prevalences are high' (Behrman & Rozenweig 2001). The portion of the global burden of disease (mortality and morbidity, 1990 figures) in developing countries that would be removed by eliminating total malnutrition is estimated by Mason, Musgrove and Habicht as over 32% (Mason, Musgrove, Habicht 2003). This includes the effects of malnutrition on the most vulnerable groups' burden of mortality and morbidity from infectious diseases only. This is therefore a conservative figure, but nonetheless much higher than previous estimates, mainly due to now including micronutrient malnutrition (Mason, Musgrove, Habicht 2003). Seen in relation to the overall disease burden (all population groups, all causes, all developing countries), eliminating micronutrient malnutrition (in children plus anaemia in reproductive age women) would save approximately 18% of the global burden of disease, with eliminating child underweight an additional 15%. This clearly has important

implications for programming and funding, but is currently not adequately communicated to policy makers, planners and donors.

3.6 Reducing poverty

This is not always explicitly addressed as an intervention in the control and prevention of micronutrient deficiencies, but if it were to be possible, would have the greatest impact of all. It is explicitly mentioned in UNICEF's State of the World's Children Report (1998a), and in the prevention of iron deficiency anaemia (WHO/UNU/UNICEF 2001) and elsewhere, but rarely proposed as a serious intervention to address micronutrient malnutrition. Following more studies on cost-effectiveness, and studies by economists such as in the reports of 'Macroeconomics and Health' and the 'Copenhagen Consensus' (both of which will be discussed further in chapter 6), this should change. It has been noted before, that Europe had a significant vitamin A deficiency problem in the 19th century that was resolved without specific programmes (Oomen 1976). Likewise the relative prevalences of anaemia between rich and poor countries make it clear how much iron deficiency and other nutritional anaemias are problems of poor diets and poverty (WHO/UNU/UNICEF 2001). These economic and development arguments for intervening in health and nutrition have an increasingly strong underpinning (World Bank 1993, Mason, Musgrove, Habicht 2003 amongst others) and have been further driven by the 'WHO Commission on Macroeconomics and Health' and the report of the 'Copenhagen Consensus'. The widespread adoption of the Millennium Development goals (chapter 4) further reflects this shift in geo-political consensus. It remains to be seen if the adequate political and economic changes will be adopted and the agenda adequately funded.

3.7 Conclusions

As noted, efficacy of micronutrient prevention and control, and treatment, is well-established. The big challenge is effective national or sub-national intervention programmes. Transition from vertical to more integrated programmes, and getting donor support for these, are a current major challenge. These will be further discussed when looking at trends over the last decades, and current monitoring and evaluation efforts. As is frequently quoted, the cost effectiveness of most micronutrient interventions (including vitamin A deficiency) continues to need advocacy to policy makers: overall, it has been

estimated that for “less than 0.3% of their GDP, nutrient deficient countries could rid themselves of these entirely preventable diseases, which now cost them more than 5% of the GDP in lost lives, disability and productivity” (World Bank 1993). Given the comparative success of many of the micronutrient deficiency prevention and control programs in many parts of the world, because of the known delivery systems, the chance of achieving the internationally-agreed goals is the implicit topic of the remaining chapters.

Chapter Four

4.0 International fora, commitments and micronutrient goals

Prompted by the magnitude of micronutrient malnutrition, the public health impact of such micronutrient deficiencies, and the demonstrated feasibility of intervening, there has been a remarkable degree of agreement on what needs to be done. Part of this consensus comes from the cost-effectiveness of the interventions, and probably, their apparent relative simplicity. This chapter looks at what actions that consensus has brought by examining: (i) international goals and agreements relating to micronutrient prevention and control; (ii) the partners involved and their roles; (iii) some of the reasons why; and, (iv) finally, how micronutrients rose to their current position of importance in the international health and development agenda. In the following chapter (five) the outcomes, progress- or sometimes the lack of it, and trends, and their relationship to the goals, will be presented.

4.1 International commitments on micronutrients: the goals and midterm goals

The public health significance of micronutrient malnutrition in the developing world was recognized and acknowledged globally in December 1992, at the FAO/WHO International Conference on Nutrition (ICN), where representatives of 159 countries and the European Common Community pledged to make all efforts to eliminate the iodine deficiency disorders and vitamin A 'before the end of this [1990s] decade', and to reduce substantially within this same decade 'other important micronutrient deficiencies, including iron deficiency' (FAO/WHO 1992).

In 1990, the U.N. held the World Summit for Children, attended by 71 Heads of State, which established broad goals for the health and well-being of children (UNICEF 1990a). The nutrition goals, including those for micronutrients, agreed to at this forum, were endorsed (with slightly different wording) at the 1992 ICN. The UN Nutrition goals of the Fourth United Nations Development Decade, incorporating the World Summit for Children Goals, included four over-arching goals:

(a) To eliminate starvation and death caused by famine;

(b) To reduce malnutrition and mortality among children substantially;
(c) To reduce chronic hunger tangibly; and
(d) To eliminate major nutritional diseases

The nutrition goals of the actual World Summit for Children (WSC) document to be reached by year 2000 (UNICEF 1990a) were more specific than the above but still ambitious. There were eight nutrition-related goals (nearly a third of all the goals) including reducing moderate and severe malnutrition in children under-5 by half of 1990 levels and reducing low birth weight to less than 10%, as well as ones on breast-feeding, growth promotion and monitoring and household food security (UNICEF 1990a, Shrimpton et al. 2002). Those specifically on micronutrients were:

- Reduction of iron deficiency anaemia in women by one third of the 1990 levels;
- Virtual elimination of iodine deficiency disorders; and
- Virtual elimination of vitamin A deficiency.

Between these two major UN meetings, there had been a special meeting on micronutrients in Ottawa in 1991, “Ending Hidden Hunger” (Micronutrient Initiative 1991) and this was perhaps the first real international recognition that micronutrients were becoming a strategic part of international public health. It aimed to promote a separate, higher profile for micronutrients, or at least the three identified in the Summit Goals. These had been identified on the basis of current (at the time), very imperfect, knowledge of the size of the problem, the impact on populations, especially women and children, and the perception, that here were nutrition goals that could be achieved. This meeting in Ottawa took a slightly different tack, as the goals had already been agreed to at the WSC in 1990, by having three ‘calls to action’, that would be the means to reach the goals by [implicitly, the end of] the year 2000. The agreed goals were:

(i) iodine
- universal availability and consumption of iodized salt
- or, iodized oil distributed to reproductive women

(ii) vitamin A
- universal availability and consumption of vitamin A rich foods
- distribution of vitamin A supplements to young children and lactating mothers

(iii) iron

- access by all pregnant women to iron supplements
- wide availability and consumption of iron-rich foods

The ACC/SCN (United Nations Administrative Coordinating Committee's Subcommittee on Nutrition) Meeting was held in Ottawa in 1993 and results included reports on controlling vitamin A deficiency (Gillespie & Mason 1994) and iron deficiency (Gillespie, Kevany, Mason 1991). At this point these were mainly about how to do implementation.

The FAO/WHO ICN the following year took a yet somewhat different approach by having a World Declaration on Nutrition (essentially nine overarching goals) and "9 action-oriented strategies". Each of these action-oriented strategies had more specific targets, generally similar to the WSC goals (FAO/WHO 1992, WHO 1993, 1995). The World Declaration on Nutrition was as follows [bolded italics added]:

"As a basis for the Plan of Action for Nutrition and guidance for formulation of national plans of action, including the development of measurable goals and objectives within time frames, we [the Ministers and Plenipotentiaries] pledge to make all efforts to eliminate before the end of this decade:

- Famine and famine-related deaths;
- Starvation and nutritional deficiency diseases in communities affected by natural and man-made disasters;
- ***Iodine and vitamin A deficiencies.***

We also pledge to reduce substantially within this decade:

- Starvation and widespread chronic hunger;
- Undernutrition, especially among children, women and the aged;
- ***Other important micronutrient deficiencies, including iron;***
- Diet-related communicable and noncommunicable diseases;
- Social and other impediments to optimal breast-feeding;
- Inadequate sanitation and poor hygiene, including unsafe drinking water".

These were followed by the nine action-oriented strategies, including "assessing, analyzing and monitoring nutrition situations".

Although many of the goals of the Children's Summit were reinforced at the ICN, this was largely at the insistence of representatives and participants, rather than a demonstration of UN harmonization. In many cases, increased technical input was apparent from the earlier UNICEF goals, with the wording of goals subtly changed to be more likely to show a success and to recognize public health realities. So, for example, the UN Summit goal in 1990 for iron deficiency anaemia had been to reduce iron deficiency anaemia by one third of 1990 levels, whereas the ICN goal was to pledge 'to reduce substantially within this decade…other important micronutrient deficiencies, including iron' (FAO/WHO 1992). Both iodine and vitamin A deficiencies were to be eliminated but the rider was added 'as a public health problem' and 'eradicate' carefully not used (c.f. smallpox). The action goals were therefore: the elimination of the iodine deficiency disorders as a public health problem; the virtual elimination of vitamin A deficiency and its consequences, including blindness; and the substantial worldwide reduction of iron deficiency anaemia (FAO/WHO 1992, WHO 1993).

At that time the participants clearly thought that establishing these goals was a practical way of moving forwards. The whole concept of global goals and their utility has since been debated (e.g. ACC/SCN 2001) and will be discussed in Chapter Seven. Certainly goals were established that virtually all affected countries have at least aimed for and with which donors in particular have felt very comfortable. From the outset there were some problems with the ICN. UNICEF had been excluded, largely at FAO's urging, on the grounds that they were not a "Technical Agency" of the UN System, unlike FAO and WHO. This was not a good start, especially as UNICEF ended up funding the attendance of many participants, and would be the main implementers within the UN system, at country level. FAO and WHOs already grudging cooperation between themselves did not last far beyond the ICN, and had in fact, shown early strains in the PrepCom (Preparatory Committee) held in the Palais des Nations in Geneva some months before the actual ICN) with bickering over wording and procedural matters (author, personal communication).

Following the ICN, at which countries had committed themselves to developing National Plans of Action for Nutrition (NPANs), countries not infrequently had visits from FAO consultants advocating a National Plan of Action (NPAN) - often called a National Food (Security) Plan, followed a couple of months later by a WHO team advocating, even if

not directly, a National Nutrition plan that emphasized health and nutrition. The other criticism from countries at that time was that the consultancy advice was extremely formulaic, following closely the nine strategies listed in the ICN Plan of Action, irrespective of need and priorities of the countries. This was largely on instructions from the agencies, especially FAO, which had taken the lead all along from a somewhat apathetic WHO at the time, (with some notable personal exceptions). Fortunately, this state of affairs improved after a few years when greater cooperation between all agencies took place, partly urged on by the UN Reform Agenda of the Secretary-General, but also by changes in personnel at the agencies. One outcome of these changes was a greater harmonization between WHO and UNICEF in health and nutrition matters as e.g. in the mid-decade goals (Shrimpton et al. 2002).

Nevertheless, more than one country counterpoint has pointed out the irony of being encouraged to develop a 'multi-sectoral plan of action for nutrition' when those pushing hardest for it did not seem particularly successful at multi-sectoralism and cooperation themselves. On the other hand, there were frequently times when this became a useful leverage for countries, in that it meant greater resources were available to countries (the competitiveness often dexterously managed by governments to their advantage). This was probably less of a problem for the micronutrient goals, which were managed in a fairly vertical manner, especially at national level. Nevertheless this lack of integration still happens, even within Agencies, as for example the proposed global strategy for infant and young child feeding did not mention micronutrients, presumably because a different 'cluster' (section) within WHO handles micronutrients (WHO 2001a). As noted, the poor collaboration between agencies became less of an issue over time, as some degree of 'task allocation' took place, and more 'players' became involved in funding nutrition interventions, especially USAID (e.g. by funding the OMNI- Opportunities for Micronutrient Interventions- Project through John Snow Incorporated and currently the MOST Project- Micronutrient Opportunities for Strategic Targeting, only the acronym itself was retained- through ISTI Inc.) and Canada's International Development Agency, CIDA/IDRC (e.g. by generously funding the Micronutrient Initiative and UNICEF vitamin A activities). Over time, and reflecting what was commonly seen as a partial vacuum in nutrition at both FAO and WHO at the time, other players took larger roles, such as UNICEF taking a more 'technocratic' role (Shrimpton et al. 2002), and the World Bank playing an ever larger role, especially in establishing the cost-effectiveness of

micronutrient interventions (Miller Del Rosso 1992, McGuire & Galloway 1993, Prah Ruger 2005).

Nevertheless, a couple of years after the ICN, it was becoming clear that very few of the goals would be reached, and if any were, it would be in only a few countries. This is not to say that no progress was made as there were declines in infant mortality rate (IMR), rates of low birth weight (LBW) and less so, but real declines in the prevalence of undernutrition (ACC/SCN 1997b). This progress was, however, uneven across continents and countries and too slow to expect that the global goals would be reached. Considerable progress was being made in reducing the prevalence of the iodine deficiency disorders (IDD) as measured by the process indicator of salt iodization and moderate progress in vitamin A, as measured by vitamin A capsule coverage. Virtually no progress was being made in the reduction of global levels of iron deficiency and anaemia in general (ACC/SCN 1997a, ACC/SCN 1997b, Mason et al. 2001, SCN 2004).

Consequently, largely at the urging of UNICEF, in a special session of the Joint UNICEF/WHO Committee of Health Policy, it was decided to identify a series of mid-decade goals that would largely be tracked by UNICEF Country Offices (UNICEF/WHO 1994a, b). Most notable is the absence of a mid-decade goal for iron. Iodine was largely to be addressed by the process goal of levels of salt iodization in countries because of the assumption that with adequate universal salt iodization (USI), IDD elimination would inevitably follow. The actual mid-decade goals were:

- 'Universal salt iodization in IDD-affected countries (90 per cent or more of food-grade salt iodized or more than 90 per cent of households consuming iodized salt)'; and,
- 'Ensure that at least 80% of all children under 24 months of age living in areas with inadequate vitamin A intake receive adequate vitamin A through a combination of breast-feeding, dietary improvement, fortification and supplementation'.

The vitamin A mid-decade goal was more difficult in that 'adequate vitamin A', including dietary adequacy was to be the goal, although it was not clear how this would be ascertained. How for example, could a country assess the contribution to total vitamin A adequacy if the country had some vitamin A fortification, some supplementation

activities and promotion of dietary diversity programmes, in a way that could be categorized? The indictors were biochemical, histological and functional, for example XN (night blindness). A problem for the usefulness of both the mid-decade goals was that they, probably by necessity, were national goals with no indication of more vulnerable sub-populations. The third mid-decade goal was on breast-feeding promotion through the Baby Friendly Hospital Initiative.

These mid-decade goals were partly a response to a perceived lack of continuing acceleration of activities, and the wish of the then Executive-Director of UNICEF, James Grant, to see the goals achieved before the end of the decade, the original aim (and possibly because of the knowledge of his own terminal illness). The fact that iron did not have a mid-decade goal probably reflected a lack of consensus but also the early recognition that the goal would not even nearly be met. It also reflected that 'there was no clear solution to the technical and operational problems that traditionally hamper progress' (UNICEF/WHO 1995). The thirtieth session of the UNICEF-WHO Joint Committee on Health Policy subsequently tried to remedy this by releasing a document on a suggested '[s]trategic approach to operationalizing selected end-decade goals: reduction of iron deficiency anaemia' (UNICEF/WHO 1995), noting that only limited gains had been made in only a few developing countries. Some recommended actions were made including that 'by the end of 1995, all countries where IDA during pregnancy and/or in pre-school children occurs in excess of 20% of the population should have national plans of action for nutrition that include a specific programme for preventing and controlling IDA and iron deficiency…' (UNICEF/WHO 1995).

In reality the development of these mid-decade goals meant a flurry of country activity (mainly in UNICEF Country Offices) and no doubt helped the institutionalization of monitoring processes. However, it seems unlikely than it ended up being much more than a data collecting exercise to show 'progress'. A massive evaluation process was continued in the build-up to the UN Special Session on Children planned for 2000 and provided much valuable information on the progress or otherwise towards the goals (UNICEF 2001a,b).

At the same time, WHO and FAO were separately monitoring progress on the goals, especially the adoption of national plans of action for nutrition (WHO 1995). At the

same time, WHO was building and considerably refining the databases on IDD, vitamin A and iron. These built on earlier publications of databases from WHO such as the micronutrient deficiencies information systems- MDIS I (iodine in 1993) and MDIS II (vitamin A in 1995). Again it is noticeable that an iron publication did not come out. A report from an expert group (WHOI/UNICEF/UNU) held in 1993 took over eight years to be published by WHO, despite containing sorely needed guidelines and cut-off points (WHO 2001b). Concurrently UNICEF, with Tulane University and MI were conducting their own report, using MICS (the Multiple Indicators Cluster Surveys of UNICEF), as a lead-in to the end of the decade, and subsequently UNGASS (the United Nations General Assembly Special Session on Children) planned for 2001. It had earlier devoted its 1998 'State of the World's Children' annual report to nutrition, including an emphasis on micronutrients (UNICEF 1998a, 1998b, Mason et al. 2001).

One of the most important international agreements, although only relatively recently gaining attention as a tool for nutrition issues is the Universal Declaration of Human Rights- the UN resolution of 1948 (UN 1948). Amongst other worthy rights is Article 25 which states that everyone 'has the right to a standard of living adequate for the health and well-being of himself and of his family, including food…' and that 'motherhood and childhood are entitled to special care and assistance' (UN 1948). These legal rights have been accepted by the vast majority of the international community and articulated in a series of international conventions including the Convention on the Elimination of All Forms of Discrimination against Women (UN 1979) and the Convention on the Rights of the Child (UN 1989). Very recently, water has been added as a human right. UNICEF, as a special fund of the UN System, built on this basis when it held the World Summit for Children (WSC) in 1990 in that it emphasized goals to drive development and shape actions. It also added another measure (achievement of the right) against which to measure progress. The 1990 WSC document and its goals were impressive in the range of health and protection aims, with a large number of goals relating to health and nutrition, and rightly recognized, that without adequate health and nutrition, many other aims would not be feasibly reached. This was a somewhat new idea at the time when health and nutrition were seen as outcomes, rather than as necessary inputs (as they largely are today e.g. Sachs 2001).

International agreement on making micronutrients a priority, and the various actual goals agreed to, are part of an increasing trend over the last several decades to use the

political global summit approach to health and other related issues, hunger, the environment and so forth. In an increasingly more connected, more complex, and perhaps more uncertain world, the holding of global fora are seen as a way of focusing attention, and hence national commitments and then funding, on health and nutrition issues. While partially successful, it may, as recent experiences with the FAO World Summit +5 (FAO 2005a) and the Sustainable Environments and Development Rio+10 (UN 2003) suggest, be losing impact and effectiveness. It may be that these international fora have outlived their usefulness in provoking some action and commitment from the more affluent nations. It is clear that donor countries, for many reasons, are not honouring the commitments made at these meetings. For example, the increased aid required to meet the Millennium Development Goals (MDGs) promised at the International Conference on Financing for Development at Monterrey in 2002, had not yet been delivered in 2005 (Sachs & McArthur 2005) and major shortfalls remain. This clearly limits their usefulness. It has been noted that the lack of real progress must raise fundamental questions about political commitment, especially by the leaders of the rich nations, of the way, and even the real intention, to build a global sustainable and equitable future. This also begs the above overall question of the continuing usefulness of such international gatherings (Hewett 2002). It may be that their greatest use is to develop consensus on goals.

It remains to be seen whether the recent report of the Millennium Development Project (building on the Monterrey Conference above and chaired by the economist Jeffrey Sachs of Columbia University in his role of special adviser to the U.N. Secretary-General) which asks for considerable transfer of funds to the Developing World will be any more successful (UN Millennium Project 2005, Fleck 2005). There are some encouraging steps such as the UK government using its presidency of the G8 and the EU to push for a significantly expanded effort to tackle poverty in Africa. However, until the USA and others, including Australia, improve their relatively miserable aid contribution, success is unlikely to be achieved. The findings of the Copenhagen Consensus, given the team was made of somewhat conservative economists, is encouraging. In their recent report, the resulting ‘Copenhagen Consensus’, coming from the panel of economists setting priorities among a series of proposals for confronting ten major global challenges, prioritized the use of a hypothetical $50 billion made available to governments in developing countries. Providing micronutrients

through a combination of public health and private sector programs was ranked second, after control of HIV/AIDS (Behrman, Aldermann, Hoddinott 2004).

In terms of the micronutrient goals already endorsed and committed to, come the end of the decade and the century (however defined), those goals, including the micronutrient goals, had clearly not been met at a global level. Nevertheless, much progress had been made (as will be outlined in Chapter 5). There was enough consensus of the utility of such goals for new ones to be put forward as the 1990s decade drew to a close, although content and wording provoked some controversy before the actual wording could be agreed upon, especially for iron (and even if there should be another goal for iron at all). Nevertheless, the micronutrient goals emerging from the earlier three international fora and endorsed at many other international and national scientific meetings, were re-affirmed and extended at a UN Special Session on Children held in May 2002 (delayed from September 2001 because of the destruction of the World Trade Center buildings in New York on September 11, 2001). But these affirmations were not without some continuing controversy; especially the initial absence of a food-based strategy as one of the ways of achieving the goal (but which subsequently was added late in the proceedings). The current goal is to "achieve sustainable elimination of iodine deficiency disorders by 2005 and vitamin A deficiency by 2010; reduce by one third the prevalence of anemia, including iron deficiency, by 2010; and accelerate progress towards reduction of other micronutrient deficiencies, through dietary diversification, food fortification and supplementation" (UNICEF 2001b).

4.2 The roles of the many 'players' involved

The three delivery mechanisms mentioned- dietary diversification, food fortification and supplementation, as well as other public and socio-political support- require active partnerships for successful and sustainable implementation. At a minimum these consist of national governments, international and multilateral agencies, international consultative groups, bilateral agencies, plant breeders, international NGOs/PVOs, national NGOs, individuals, and increasingly, the private sector. Sachs and McArthur (2005) refer, somewhat optimistically, to a 'country's international partners- including bilateral donors, UN Agencies, regional development banks, and the Bretton Woods institutions' which they say should be giving 'all the technical and financial support needed to implement the country's strategy'. Others, such as Richter, urge some

caution in even the use of the word ‘partnerships’, given the very different operating modalities and expected outcomes of the public and private sectors, especially in low income countries (Richter 2003). Nevertheless, many such collaborations are essential as e.g. in the iodization of salt.

For this discussion, the chapter will continue to mainly address vitamin A, iron and iodine as these have received most attention to this point, and are the ones that have their specific international goals (FAO/WHO 1992, UNICEF 1990a, UNICEF 2002a,c), although zinc and folate are increasingly on the global micronutrient agenda. To some large extent, if these initial three could be satisfactorily addressed, especially using food-based approaches, most of the other micronutrients would anyway also be covered. One of the recurring themes of public health is that there is no single intervention, no ‘magic bullet’ that will completely address the control and prevention of a disease. Even immunization needs the support of good nutritional status to be most effective, as well as good sanitation and environmental improvement. In the same way, and perhaps even more importantly for addressing micronutrient malnutrition, it has been repeatedly suggested, interventions need to be implemented as a multisectoral partnership, using several approaches, to be most effective (Darnton-Hill 1997, Darnton-Hill 1998a, Darnton-Hill 1999a, WHO 2001a). The comparative advantages of the different partners have also been somewhat described before, including at the ‘Ending Hidden Hunger’ meeting, indicating an early strategic choice, particularly for the North American partners (MI 1991, Darnton-Hill 1997, Darnton-Hill 1999b).

National governments are the main party involved in terms of on-going policy, programmes on the ground such as in rural health centres, and ultimately, sustainability. The priorities of funding agencies can direct action for a limited time (for better or worse), but will still need government conviction and support for national success and for sustainability (Tagwireyi 1994). Nevertheless, micronutrient programmes in developing countries have not infrequently been perceived as donor-driven programmes (Arthur 2001). They (National Governments) are also ultimately responsible (sometimes pending external funding) for policy, commitment, and career and financial rewards to ensure this commitment, facilitating legislation and sustainability by including budget line items for micronutrient activities. With the move towards decentralization of many health systems, districts more often have the implementing role, but still require central support. As

Houston has pointed out: (Houston 2002) '[W]hile Ministries of Health define health policy, and thus the policy on vitamin A interventions, it is Districts that implement these policies'. In the words of T.E Lawrence, in a very different context: 'Better to let them do it imperfectly than [try] to do it perfectly yourself, for it is their country, their way, and your time is short' (Lawrence quoted in Packer in the New York Times in 2003). The remaining crucial element is the government's own health and nutrition personnel working at community level who are the ones usually responsible for getting micronutrients, through nutrition education, supplements and associated health care to those in need. Where this is not yet happening effectively, often because of lack of health system resources, or poor governance, national and local NGOs often play a vital role in addressing these needs.

The international, multilateral agencies, in particular UNICEF, WHO, FAO, increasingly the World Bank, and others such as UNDP and WFP, play an essential role. UNICEF plays a role by having offices in virtually all low to middle income countries and through their influence on health, nutrition and development plans of countries, as well as supplying of supplements (from CIDA through MI), but also more recently with a great deal of technical and programmatic support, especially the global effort in IDD elimination. It is unlikely that without the UN (through UNICEF) having micronutrient malnutrition as a Summit Goal that much of what has happened would have taken place. The FAO/WHO ICN goals have been able to build on this. More recently, with an increasing agreement on action, most countries now receive the same message from their UN colleagues, although emphasis often differs at country level. Credit should also go to the (often under-appreciated and under-funded) ACC/SCN (Administrative Coordinating Committee's Subcommittee on Nutrition) of the United Nations system (now the Standing Committee on Nutrition) which has pushed the UN Agencies, and lately the Bilateral Agencies and Civil Society NGOs to have a more coordinated response, although its influence has gone up and down over the years. This it does through thematic Working Groups and published reports, including the publication of the State of the World's Nutrition Situation. No longer a UN Subcommittee, its role is evolving, but will to a large extent depend on the goodwill and commitment of the UN Agencies, and bilateral funding agencies. Any role of the private sector, apart from just attending, continues to be roundly debated within the SCN (author, personal observation 2005).

WHO has been able to use the World Health Assembly resolutions as an important advocacy tool at national level and by its continuity of low level sustained input in training and national programmes. Its important roles in normative setting and global database maintenance are similarly important. FAO is now more fully embracing nutrition as an essential component of agriculture and food security, as is the WFP (World Food Program) with its role and growing influence in the increasing number of emergencies worldwide. FAO was the lead agency for a 10 year vitamin A push which started in the mid 1980s but was before its time, and, as it was relying on extrabudgetary funding which did not come forward, it was not very effective, but helped set the scene for awareness of micronutrient malnutrition as a global problem to be addressed. Agencies also have their own priorities which can sometimes take precedence over country needs. While their effectiveness sometimes has been questioned, the normative role of WHO, the programme and policy strategies of UNICEF, and the regard in which these organizations are held in-country has ensured their critical role.

The World Bank filled something a vacuum in nutrition at WHO and FAO in the early 90s at a time when it published the small but influential “Enriching lives’ about overcoming vitamin and mineral malnutrition in Developing Countries (McGuire & Galloway 1994) and then subsequently published, with WHO, the global burden of disease using the DALYs (disability life adjusted years). The World Bank’s role continues to expand in international development and global public health and nutrition (Prah Ruger 2005) and it is unclear where it will go now with the new president (who at time of revision is being urged to resign over corruption and other issues - and finally did). Nevertheless, its recent publication on repositioning nutrition in development programmes (World Bank 2006a) has been quite influential, largely because of the perceived clout of ‘The Bank’. UNICEF had also lost positions in nutrition over the last few years of 1990s and early 2000s, especially at Country office level, although this has recently been somewhat reversed and the current Executive Director has made it clear that she sees nutrition programmes and policy as integral to where she sees UNICEF going in terms of impact, and progress towards the MDGs. On the other hand, WFP has strengthened its nutrition component, including micronutrient fortification of the foodstuffs it shifts around the world to places experiencing food shortages, especially in emergencies. Global alliances such as GAVI (Global Alliance on Vaccines Initiative), The Global Alliance against TB, Malaria

and AIDS, and GAIN (Global Alliance to Improve Nutrition), have become increasingly important (often with Bill & Melinda Gates Foundation funding). While these global alliances may have drawn resources away from UN bodies, especially UNICEF, WHO and UNAIDS, they may also represent truly increased international budgetary resources. Virtually all the global alliances have been funded at levels lower than originally anticipated, and their effectiveness in terms of micronutrient goals are discussed further below. Their effectiveness is increasingly being questioned, as is the costs of their need to set up separate administrative structures (sometimes at the behest of the funding agency's government, as in the USA government and the Global Fund). The role of the UN Agencies in IDD elimination has recently been published (Dalmiya et al. 2004) in the updated Hetzel volume (2004).

The bilateral agencies have also been extremely important, probably essential. AusAID has been supportive in a sustained way of ICCIDD as has, on a larger scale, Canada (through CIDA), the Netherlands and others, particularly the Nordic countries. USAID has been a strong and consistent supporter of vitamin A in particular, but also iron and iodine, and in the future probably zinc. CIDA is now the main supporter of vitamin A activities, especially through its donation of vitamin A capsules to UNICEF through the Micronutrient Initiative. Committed or ear-marked funds from a bilateral agency can sometimes be the essential engine that initially starts a national programme or drives a special attention to micronutrient malnutrition. Another mechanism that the Bilateral Agencies have used is to have specialized contracts, such as the OMNI and MOST projects of USAID, or the Micronutrient Initiative (MI)- a project largely funded by Canadian CIDA (with UNICEF, World Bank and other input). The funding by Canada, the Netherlands, the Scandinavian countries, the UK and the USA through INGOs and national NGOs and sub-contracted commercial and other non-profit (but expensive) development cooperative agreements have been vital to success. Bilateral government involvement, often a different agency or division section from that dedicated to aid e.g. USDA (United States Department of Agriculture), are also very important in ensuring aid supplies are properly fortified with micronutrients. Nevertheless, such bilateral aid certainly has the potential to make health and nutrition activities in resource-poor countries, 'donor-driven' i.e. the funds determine the programmes that can be launched, irrespective of the needs as determined by the Government, which maybe spending less than $US5 annually a head on health. A further criticism has been the relatively short

time frame of some of this funding e.g. the USAID 5 year cycle. If CIDA was to change its priorities from vitamin A, many of the vitamin A capsule programmes would likely collapse in many low income countries.

Besides the UN Agencies, special interest NGOs such as the International Vitamin A Consultative Group (IVACG) and the International Council for Control of Iodine Deficiency Disorders (ICCIDD) have played crucial roles in raising the awareness of micronutrient malnutrition of international agencies and national ministries, through a combination of providing technical input, funds, research funds for early epidemiological and/or pilot interventions and special high-level advocacy (Hetzel 2005). These international consultative groups have been major players in the effort, in a way that may be somewhat unique and have lessons for other public health strategies. They have included the International Council for Control of the Iodine Deficiency Disorders (ICCIDD), the International Vitamin A Consultative Group (IVACG), and the International Nutritional Anemia Group (INACG) and more recently IZiNCG. There is also now an increasing interest in folate/folic acid, vitamin B12, selenium and others (UNICEF/WHO/UNU 1999, Brown & Wuehler 2000), but which will be unlikely to lead to another consultative group. In fact there is likely to be some amalgamation of the consultative groups under an umbrella micronutrient body (Davidson personal communication 2005), which had its first joint meeting as the Micronutrient Forum in Istanbul in April of 2007. This is somewhat in line with the parallel trend of advocating for supplementation, and fortification, using multimicronutrients formulations, given that micronutrient deficiencies are unlikely to occur in isolation (Huffman et al 1998, UNICEF/WHO/UNU 1999, Gross 1999, SCN/UNICEF/WHO 2006).

These consultative bodies have been enormously important in bringing both technical expertise to a point where it can be used by countries, and by advocacy which has brought micronutrients onto the national and international health agenda.

(i) ICCIDD has done this by redefining goitre as the wider spectrum of iodine deficiency diseases and demonstrating thereby a far greater potential impact of iodine deficiency on health and development (ACC/SCN 1997b, ICCIDD 1998, Hetzel et al. 2004, Dalmiya et al. 2004). It has also maintained a high level of persistent advocacy, including skillful use of the WHA resolution mechanism mentioned above.

(ii) IVACG, largely supported by USAID, has been successful in much the same way but using somewhat different mechanisms (e.g. relying on generous funding from USAID for country activities and by supporting research and technical excellence, especially through Johns Hopkins University) but has used the UN less. An international IVACG meeting every 18 months has been an important dissemination mechanism, especially to bring together implementing ministries, NGOs with vitamin A programmes (e.g. operational research such as that done in countries by Helen Keller International), and the academic scientific community.
(iii) INACG has been less successful than the other two for a variety of reasons- one of which appears to be a lack of unanimity among iron experts on the best way to proceed, partly it is suggested because its prevention and control activities were over-medicalized in conception (Viteri 1998, Yip 2002).
(iv) Although there is recent evidence of INACG playing a more effective role, a perceived gap is being attempted to be filled by IDPAS (the Iron Deficiency Project Advisory service), a project of the International Nutrition Foundation (INF) and the United Nations University (UNU) that receives primary support from the Micronutrient Initiative (MI) and sits at Tufts University in Boston, USA. Using electronic access through web pages and so on, it provides advice and a diverse set of documentation related to micronutrient malnutrition with an emphasis on preventing and controlling iron deficiency anaemia (www.micronutrient.org/idpas/).

The stated aim of such consultative groups is to facilitate the incorporation of science into programmes. As mentioned, with an increased attention to multisectoral approaches and the reality of single micronutrient deficiencies being relatively rare, their role may have already peaked. However, both donor governments and academics in their particular field find great utility in such a vertical, but often effective, approach. As noted, IVACG and INACG have recently been merged as the Micronutrient Forum, partly reflecting an emerging international consensus towards integration, especially in delivery of child survival programmes following the Bellagio Child Survival Study Group articles in the Lancet (e.g. Black, Morris, Bryce 2003).

The Micronutrient Initiative is now an international NGO but still functions as quasi-transnational body, in the manner of the International Food Policy Research Institute (IFPRI), a part of the international CGIAR complex, although the former was originally

established as a secretariat operating within the Canadian International Development Research Centre (IDRC). Its self-described mission is to stimulate and support national actions to eliminate micronutrient malnutrition, assuring universal coverage and sustained impact on the health and well-being of people (www.micronutrient.org). The MI has played a pivotal role in micronutrient malnutrition, especially in materials and education, but also in field research into innovative interventions but as with other agencies and institutions, its reputation and effectiveness has waxed and waned, but is currently re-focussing on its traditional strengths. IFPRI has also played a major role in testing and evaluating interventions and the policies behind them, and especially the determinants of the problems, at the country level, often in multi-country studies. The mission of IFPRI is to identify and analyze policies for sustainably meeting the food needs of the developing world, with a particular emphasis on economic growth and poverty alleviation in low-income countries, improvement of the well-being of poor people, and sound management of the natural resource base that supports agriculture (www.ifpri.org).

While the public sector and governments could be argued to be the most essential in terms of the sustainability of programmes over the long term, academia has played a major role over the last 30 years at least (e.g. see history of vitamin A research in Semba 1999, Semba 2001b, West & Darnton-Hill 2001). Nevertheless, there is still a surprising amount not known about the control and prevention, and even basic physiology, of micronutrients. There is still not agreement e.g. on the best dosage regimen for iron tablets (Stoltzfus 2001b), or exactly how vitamin A acts to reduce mortality (Sommer & West 1996), or whether multiple micronutrients have a role, and if so, in what combination and dosage e.g. in the prevention of low birthweight (Friis et al. 2004), or in delaying the transmission of HIV infection to AIDS (Fawzi et al. 2004a). The interface between universities (and sometimes donors, especially in North America) has been to translate emerging scientific knowledge in a way that could be tested in the field, and subsequently adapted to public health programmes. International NGOs such as Helen Keller International, and USAID-funded projects such as OMNI and MOST, have played a critical role, often with a university partner such as Johns Hopkins, Harvard, U.C., Davis (University of California), Emory Universities in the USA, University of Southampton in the UK and Wageningen University in the Netherlands, amongst others. They have done this by taking existing and new academic scientific information, testing it

in pilot studies for both efficacy, and effectiveness, and subsequently translating it with governments into larger, and even national, programmes.

While playing their traditional roles, some academic institutions have been instrumental in the emergence of a particular micronutrient, e.g. Johns Hopkins University for vitamin A from the early work in Indonesia and since then Nepal and other important sites such as Bangladesh and Tanzania. Harvard University has played an important role in micronutrients and HIV (building on earlier work of Semba 1993). Many others have been important, including Wageninen in the Netherlands, Tulane and Cornell in the USA, and the Institute of Child Health at University of London and many others. Many other universities, including those in other parts of the world (e.g. Sweden), have worked on the biochemistry and physiology of the different micronutrients, essential to develop policy and programmes. Special institutions such as the US National Institutes of Health, the UK MRC (Medical Research Council- especially in vitamin A and general undernutrition in Ghana), and the Australian CSIRO (Commonwealth Scientific and Industrial Research Organization), especially in the early iodine work, and to a lesser extent, zinc. The whole imperative is to bring the findings of research to the development of policies and strategies, and then to the implementation of programmes. A further important need is to raise the capacity and involvement of universities in resource-poor countries (where most of the research being discussed here actually takes place).

International NGOs/PVOs have also played a large role. In particular, Helen Keller International (HKI) with vitamin A and other micronutrients with generous USAID, and other, funding; World Vision with Canadian funding, the Program against Micronutrient Malnutrition (PAMM) out of Emory University; CARE, and the Kiwanis International generous support, especially to UNICEF, for IDD elimination activities, and others have often been key to the success of global and national programmes. In a review by questionnaire of Private Voluntary Organizations (USA-based International NGOs), four general goals were developed, and which might suggest particular strengths. They were: (i) building sustainable systems through institutional strengthening and continuing services; (ii) increasing impact by increasing program scale and quality; (iii) leveraging NGO resources by increasing local control, legitimacy and mutual learning; and (iv) increasing program efficiency by saving time, money and meeting donor requirements (USAID 1998). To these should be added two others: (v) providing a framework within

countries to allow governments and other agencies to test cost-effective approaches to much-needed innovations in public health interventions; and finally, (vi) providing a "multiplier effect" whereby those who are direct beneficiaries of interventions spread the benefits to others (Darnton-Hill 1999a). Helen Keller International's Bangladesh gardening programme has provided training and technical support to 32 national NGOs over the past 6 years. These NGO partners have implemented the project in 150 of the 460 sub-districts in Bangladesh, reaching 650,000 households, or about 3.5 million beneficiaries (Talukder et al. 2000), and is now something like 800,000 households. This would not have been possible without a broad partnership.

These international NGOs have also had a large role in providing infrastructure in-country for the effectiveness surveys, and for providing unbiased, but critical, information such as the health and nutrition surveillance systems in Bangladesh, and more recently by tracking the economic crisis in Indonesia (HKI 2000, Bloem & Darnton-Hill 2001b, Bloem, de Pee, Darnton-Hill 2005). More recently there continues to be a re-definition of how public health personnel see the private sector as an equally essential partner in terms of self-sustaining continuity as e.g. in fortification (MI 1991, Darnton-Hill 1998b, Mannar 2003) and the rise of 'Global Initiatives' outside the U.N. system such as GAIN (the largely Gates Foundation and USAID-funded Global Alliance for Improved Nutrition). These structures have their critics both within the U.N. (as they may effectively be diverting resources which might have gone to a U.N. agency, as noted earlier) and without, for perceived inappropriateness that helps the private sector part rather than the public beneficiaries (Richter 2003a,b, Chopra, Galbraith, Darnton-Hill 2002).

National NGOs have been critical players, in both delivering health care and field-testing different approaches, e.g. home-gardening in Bangladesh (as in the partnership of over 30 local NGOs, the government, and HKI described above) (Talukder & Bloem 1993, Talukder et al. 2000). Particularly in settings in which government infrastructure is not strong, or micronutrients and other nutrition activities are not seen as important interventions, local NGOs are the ones who have been getting supplements out to those who need them e.g. in Nepal (UNICEF 2003b) and West Africa (Sifri et al. 2002). Sustainability has generally been impressive where there is a sense of local ownership, and perceived advantage to the participants. Approaches involving micro-enterprises

and home gardening approaches have been particularly effectively carried out by local NGOs often with support from international NGOs e.g. Oxfam (Oxfam-Community Aid Abroad in Australia), NORAD and others. Such National NGOs work in affected countries by delivering supplements to underserved communities, home gardening activities, micro-enterprises, amongst other development activities. Funding is always an issue, as are the setting of external priorities (often those of the funding body), short time spans for programme development and implications of this for sustainability once external funding finishes.

Nevertheless, it is often at this level, and local government level, that the single, vertical approach implicitly pushed by many of the other partners, finds context within a broader, and likely more sustainable, development approach. It is also at this level that vertical programmes can come together to over-burden the final 'supplementer' at the community level, the local health worker. Nevertheless, the use of trained, often illiterate Female Community Health Volunteers, in Nepal, has been spectacularly successful in ensuring the coverage of vitamin A supplements in a country with often difficult terrain, and lately politics (UNICEF 2003b). There has been greater or lesser success with this approach and seems to depend on the local cultural norms, but seems to be again finding the favour of international donors, especially in attempts to reduce neonatal deaths through birth attendants (Lawn, Cousens, Zupan 2005)

Individuals can have a strategic impact globally, and are often a prerequisite nationally. These are the people who tirelessly advocate and keep progress on track and a priority in-country, even with the many competing claims on government resources. It is arguable, from the author's country experiences, that this is an essential ingredient for success. It has been helpful to have as advocates, presidents (Philippines) and princesses (Thailand) involved as in Asia, and the First Ladies of North and South America. The idea of involving African First ladies more in micronutrient activities is currently being advocated (Darnton-Hill, personal communication from UNICEF ESARO Nutrition Network meeting, 2004). Individual advocates that spring to mind are Solon in the Philippines (especially vitamin A), Tu Giay in Vietnam (micronutrients and nutrition in general), Hetzel in Australia (iodine deficiency disorders) and Scrimshaw of the USA in iron deficiency anaemia. More are needed.

Although the private sector has long played an essential role in fortification e.g. salt, margarine and oils, breakfast cereals and the like in the Western countries, they are only relatively recently being seen as an important partner in the developing world (MI 1991, Darnton-Hill 1997, Darnton-Hill 1998b, Bishai & Nalubola 2002, Mannar 2003). While both the public and private sectors will continue to have somewhat different agenda and roles, sustainability, at least in fortification, will not be ensured without an active partnership with the private sector, as it is the food industry that does the fortifying. A role for the private sector at village and town level shops and stores in delivering iron and folate supplements are being tested in several countries, and actively promoted by several of the donors. The role of public/private sector interactions and partnerships continue to be critically appraised, largely because of the great need of funding by public bodies, with increasingly less coming from governments, and the differing priorities and objectives of the two, and often more, 'partners' (Buse & Walt 2000, Richter 2003a). Nevertheless, one of the most vaunted examples, the Network for Sustainable Elimination of the Iodine Deficiency Disorders, which includes representatives of the Salt Industry, has yet to live up to its potential and was recently evaluated to strengthen its performance, although its usefulness is still in doubt some years later in 2007. Public-private collaboration is being facilitated by such groupings as the Flour Fortification Initiative (FFI) funded by CDC and MI out of Emory University, and, probably appropriately, dominated by the private sector such as the Australian and Canadian Wheat Boards, Milling Associations and so on (FFI 2005). There have been a series of pilot projects, especially with USAID promoting social marketing, to use the 'market place' to sell micronutrient supplements (OMNI 1995), including iron/folate (Cavalli-Sforza 2004, Cavalli-Sforza et al. 2005) but these have yet to be scaled up successfully in a sustainable way

The roles of Foundations have included providing important funding, especially to NGOs in the past, but now increasingly to Global alliances, Global partnerships and Universities, in much larger amounts. The Bill and Melinda Gates Foundation has been a significant donor to IDD activities through UNICEF. The relatively new GAIN (Global Alliance for the Improvement of Nutrition), largely funded by the Bill and Melinda Gates Foundation (US$50 million over 5 years but recently increased following a change in leadership and expansion of mandate to infant and young child nutrition). Initially this partnership was to be with the World Bank Group, UNICEF, WHO, the Governments of

US, Canada, Japan and Germany as well as transnational food corporations Proctor and Gamble, Heinz and Unilever, and the pharmaceutical company Roche (World Bank, accessed 2002, Zimmerman 2002). Currently however, the funding is effectively from the Gates Foundation and USAID. It is along the model of multilateral, bilaterals and private sector partnerships such as the Global Alliance for Vaccines Initiative (GAVI) and was launched at the UNGASS (United Nations Special session on Children) in 2002. While undoubtedly a welcome source of funds and multisectoral cooperation, the differing administrative and bureaucratic procedures, and individual institutional priorities took a long period of teething problems and are still in a state of evolution. The new leadership has the confidence of the two donors. The main aim of this particular alliance of public and private sector partners was largely to 'leverage cost-effective food fortification initiatives' (GAIN, accessed 2006), although this mandate has just been expanded to infant and young child feeding which nevertheless appears to mainly be directed at fortified complementary foods. The Gates Foundation is promising further funds for nutrition activities. Although it is stated, in a World Bank website that the fund would make grants to developing countries in support of food fortification and 'other sustainable micronutrient interventions' (World Bank, accessed 2002), it is clear that fortification will be the main, vertical intervention supported. Marion Nestle has called GAIN an example of a 'reductionist, single-nutrient techno-fix to a problem that is much more complex' that ignores that the main reason for malnutrition is poverty (Nestle in Zimmerman 2002). It has also been criticized in that it will presumably help shift the tastes of the poor 'towards processed foods, typically adding fat, sugar, and salt while removing needed fiber and micronutrients.' (Lappé & Lappé 2002 quoted in Richter 2003a). An extensive critique of UN-business interactions, and by extension other public/private 'partnerships', and in particular GAIN, has been published by IBFAN/GIFA (Richter 2003b). The role of such global alliances, including potential new ones within the UN, such as the WFP/UNICEF-led 'Ending Child Hunger and Undernutrition Initiative', in alleviating micronutrient malnutrition remains to be determined.

4.3 The rise of micronutrients

4.3.1 Background

The current interest in preferentially addressing micronutrient malnutrition may be explained, it is suggested, by a different perception by policy makers of micronutrients

and protein-energy malnutrition. In the early 1970s there was the so-called ‘protein fiasco’, when the international public health community seized upon protein as the magic bullet that would alleviate malnutrition (undernutrition). Many planners still wish to see, and demand from public health science, the production or demonstration of a ‘magic bullet’- a single intervention that will control and prevent malnutrition. One that can be measured precisely, with the required inputs known, and with an impact that can be predicted, and one that is hopefully not dependent upon socio-economic, social equity or political issues. It is one contention of this chapter that this search for the new magic bullet has largely contributed to the current emphasis on micronutrients and concomitant large increases in available international funding (Darnton-Hill 1999b, Allen 2000). While one may be pleased with the result, the rationale, especially to public health practitioners is probably less welcome. Nevertheless, based on outcomes, except for iron deficiency alleviation, the expectations of the funders may well be largely fulfilled, even if issues of sustainability remain uncertain.

Micronutrient interventions, e.g. with high dose vitamin A, has been described as ‘the seventh immunization’, and thus presumably accompanied by none of the physiological and societal complexities normally associated with public health nutrition. At the same time, in line with the magic bullet approach, supplementation is now seen as the first intervention to be used in micronutrient programmes. This has been more recently re-enforced by the current emphasis on vitamin A as an integral part of ‘Child Survival packages’ based on the Lancet Child Survival Series (Black, Morris, Bryce 2003, Dalmiya, Palmer, Darnton-Hill 2006). One impact of this has been a shift away from food-based approaches, despite evidence of impact and their likely sustainable outcome (Bloem et al. 1996). Other benefits of home gardening approaches compared to supplementation but often not captured, include increased income available to female heads of households, increased money spent on food for children (although not invariably), increased female child schooling, and increased empowerment of women in the family (Marsh 1993, Marsh 1997, Quisimbang & Maluccio 2000, Talukder et al. 2000, Smith et al. 2003, Darnton-Hill et al. 2005a).

The international community had, by the mid-1980s, become somewhat disenchanted with the prospects of effectively reducing the global protein-energy malnutrition problem (Darnton-Hill et al. 1998a, Allen 2000, Shrimpton et al. 2002). This was partly because of

unwillingness by national governments and donors to recognize undernutrition and food insecurity as political problems, but also the relative inability of organizations that had evolved from an aid, charitable perspective, to deal with a problem with global geo-political implications, especially when using a biomedical model. It also seems likely, that during the time of the so-called 'Cold War', any intervention that was explicitly aimed at the poor, especially one that required a serious redistribution of resources, was somewhat suspect, probably both in the West and even in the centrally-planned economies but notably in the West, where it was sometimes characterized as a socialist approach to malnutrition. Nevertheless, where such approaches were taken, such as in Costa Rica, Kerala State in India and Sri Lanka, and land redistribution in China, and the Republic of Korea, nutrition and health status improved, despite in some cases, low average incomes. In the Latin American countries, where serious inequities remained high, this did not happen for the poor, despite elaborate and complex National Nutrition Plans (Field 1987). However, enough anomalies remained, e.g. West Bengal State, North Korea to make generalizations suspect.

In the meantime, despite much thought, research, funds and effort, the problem of malnutrition, effectively measured as protein-energy malnutrition at that time, just seemed to get worse, thrown starkly in the public's face by horrific famines during the Ibo war within Nigeria, in parts of South Asia, and especially in North and East Africa and the famine in Ethiopia in 1973 following the failure of the long rains (Miller & Holt 1975). In fact, on a global level things have continued to get better, although the extent has depended on the particular region of the world. Both prevalence and numbers of underweight children have declined since 1980s, although the percentage remains disturbingly high in South Asia, and the situation continues to deteriorate in much of sub-Saharan Africa (ACC/SCN 2000, UNICEF 2006a) and rates of improvement declined in the 1990s (ACC/SCN 2000, Keith 2005). On the food security side, the 5.8 million people in the world today have, on average, 15% more food per person than the global population of 4 billion people had 20 years ago (FAO 1996). The 'on average' is the massive problem lost in such generalizations. The rate of improvement slowed again in the 1990s- ironically when this was the decade in which there seemed to be more knowledge and international meetings and attention, than ever before- at least since the above period in the mid-1970s when Malthusian concerns had greater credence (Blaxter 1986). Changing economic norms such as so-called 'economic rationalization' and one

outcome of the World Bank's structural readjustment policies seems likely to account for much of this slowdown (Lancet 1994). The 1990s has been described in a UNICEF review of progress and lessons learnt as 'a decade of great promises and modest achievements for the world's children' (UNICEF 2001b). But it could be said for whole countries also.

During this time of seeking new approaches and answers to the global problem of malnutrition the impact of micronutrient malnutrition gained increasing attention. It was also a time of new enthusiasm for global approaches, best epitomized by the series of global nutrition, and other, conferences (as described in chapter 3). The most important, in terms of initiating action was the UN system's first ever Summit for Children held in New York in 1990. However, other activities had lead to this such as the increasing attention being paid to new epidemiological findings, and re-interpretation of the impact of iodine deficiency e.g. the formation of ICCIDD in 1985 and preparation by WHO for a World Health Assembly (WHA) resolution in 1991 (Hetzel 1983, Hetzel & Pandav 1997), and vitamin A deficiency, such as the WHA resolution on vitamin A and xerophthalmia in 1984 and the work of IVACG and Johns Hopkins University in Indonesia redefining the problem (Sommer et al. 1983). In 1985, WHO had proposed a 10-year plan of action for prevention and control of vitamin A deficiency, for which FAO was to take lead responsibility. As noted above, tangible results were few, but were an indication of increasing attention to micronutrients.

Global attempts to alleviate the protein-energy problem had effectively stalled by the mid-1980s, with a perception by both governments and donors that little progress was being made (McLaren 1974, Blaxter 1986, Shrimpton et al. 2002). Aggravating this perception was the theoretical approach to national nutrition planning of the seventies and eighties (Bengoa & Rueda-Williamson 1976). To address new understanding of the multi-sectoral influences leading to malnutrition, national policies, especially in Latin American countries, became more and more complex, finally often paralyzed by this complexity and collapsing under their own weight (McLaren 1977, ACC/SCN 1990, Darnton-Hill et al.1998c, Shrimpton et al. 2002). The Soviet style central planning, while establishing far-ranging and effective health systems, also 'modernized' their agricultural systems, at great social and environmental cost, but was ultimately unsustainable. As the central planning in these countries collapsed, the national nutrition planning also fell

into disarray, leading to amongst other outcomes, a dramatic resurgence of the iodine deficiency disorders (Gerasimov 2002). Some of the Scandinavian and Northern European countries, notably Norway, did achieve a large measure of success in nutrition policy planning (Milio 1981). This may have been due to scale, and the relatively small, homogeneous population, and cultural and political norms, similar to the success of health promotion in Singapore (Cutter et al. 2001) and Finland's success with noncommunicable diseases (Puska et al. 1995).

Consequently all sorts of interpretations and interventions, short of actually improving diets and nutrition through political change and redistribution were tried then, and continue to be so, often at great expense. When these technological fixes also seemed to not make an appreciable difference (at least in the short run), the implication was often that somehow this was a fault of the countries themselves, or at least the poor themselves (this was still essentially the case with the World Bank's structural readjustment process some decades later). A part of this was the presumed ignorance and apparent lack of sophistication of most third world farmers, and the perceived need to improve farming methods, not infrequently by preaching economies of scale. The ecological, cultural and environmental costs of monocropping and heavy application of fertilizers and the outcome of the rapidly declining aquifers on all Continents are only now starting to be appreciated (McMichael P, 2001, Brown 2006).

Usually with the best of motives, scientists and nutritionists somewhat naively collaborated in this process through their advice, interpretation of the data, and proposed interventions. Three examples come to mind. Firstly the drive to 'educate' subsistence farmers. The positive side to this was that it became the golden age of research into agriculture- through the CGIAR network and national centres with appreciable multilateral and international/bilateral support. This research led to improved farming methods, higher and more resistant crops and averted famines in some cases. This investment in agricultural research and development has been going down ever since, a trend that has been predicted by IFPRI and others as inevitably leading to an increased danger of inadequate food for global needs (Rosegrant et al. 2001, McMichael AJ 2001). A negative side of this was, and still is in most countries, a push to a western model of large agribusiness type farms, which often led to subsistence farmers losing their livelihoods, as their farms were taken over and coalesced into large farms to allow for

this economy of scale that was apparently working so well in countries like Australia, Canada and the US (McMichael P 2001). On the other side of the political spectrum, farmers were also losing their farms as 'collectivization' of farms was going on in much of the then USSR, such as Kazakhstan, and in Tanzania.

Part of this trend was the 'green revolution', again a bitter sweet mixture of success and longer term unexpected consequences. There is no doubt that it allowed India to avoid mass starvation of many of its poor rural citizens. The negative consequences were both nutritional and socio-political, although both less immediately important than the widespread starvation that seemed to be inevitable at that time. The phenomenal success demonstrated that famine could be addressed, even in resource-poor countries (Khush 2001). The negative aspects took longer to recognize: monocropping with loss of biodiversity, enhanced dependency on fertilizers and pesticides, both unsustainable for many smaller farmers, and the social costs (Khush 2001). Part of the increasing urbanization of the developing world must be directly attributable to such trends (Brockerhoff 2000). Nevertheless, the Malthusian predictions were apparently thwarted just in time. The immense relief to many led to an enhanced belief in the power of science to address such issues. It is interesting that there is currently a push, in 2007, for a 'green revolution in Africa' by the Millennium Project of the Columbia University Earth Institute, amongst others, with interest and funding being attracted from the Gates Foundation and the Rockefeller Foundation in particular, amongst others.

It was in this sort of environment, on the apparently best evidence that the emphasis on protein emerged- later becoming known as the 'protein fiasco' (McLaren 1974), and again for the very best of reasons. On the positive side it allowed resources and attention to be given to undernutrition in a way that had not happened globally up to that point. On the other hand, it was also a scientific dead-end that may have delayed other more fruitful avenues, and certainly cost an enormous amount in resources. An unspecified cost was perhaps a subsequent scepticism by governments and donors that there was a scientific answer, and so a lesser willingness to devote large resources to nutritional, and perhaps agricultural, research. None of these things happen in isolation of course. At the same time, the World Wars were over (although the uncertainty associated with the threat of nuclear war remained) and the assumption was that future engagements would be fought not in Europe or the USA, and be more limited in scope,

such as the Korean War. Consequently, governments of the industrialized nations were likely to spend less on the nutritional well-being of their populations, and especially research, as war had often been a stimulus e.g. when recruits, often from poorer backgrounds and hence malnourished and short, were found to be relatively unfit. This was the motivation for the UK government's first food and nutrition policy (Boyd-Orr cited in Blaxter 1986) and fortification in the United States (Bishai & Nalubola 2002).

For the reasons above, many of which continue today, little headway has been made in seriously reducing the prevalence of undernutrition. This is despite the fact that there is little disagreement today on what the inevitable results of this will be in terms of growth, intellectual development and socio-economic progress. One encouraging sign, yet to be acted upon, is that malnutrition is an important factor in promoting economic development, and not just an outcome, although it is clearly that also (Sachs 2001). In 1974, the World Food Conference was called by FAO to discuss the reduction in global food supplies, largely due to poor harvests, combined with policy change of the USA to reduce its reserve stocks, that together had led to increased prices but also 'to a realization that the world was critically dependent on each year's harvest' (Blaxter 1986). At the end of the Conference, 127 Member States declared that '[w]ithin one decade no child will go to bed hungry, no family will fear for its next day's bread and no human being's future and capabilities will be stunted by malnutrition'. By 1996, when the World Food Summit was held, there were still 840 million children and adults considered hungry and at this point, Member States declared that the goal was to halve this number by 2015 (FAO 1996). A recent estimate by UNICEF gave a figure of nearly 150 million underweight (by weight for age) globally (UNICEF 2006a). However, this is not to criticize the UN Agencies, who can only carry out what the Member States give them the resources to do, and allow them to do. The failure of will is clearly with the Member States i.e. all of us and our countries.

Five years later at the WFS+5, the numbers were much the same (declining by only 2.5 million a year). This is clearly better than no improvement, but a rate far too slow to achieve the new 2015 goal. It is of further concern that China was responsible for approximately a half of any decline (~74 million people while rest of world increased by 80+ million). Besides the needs of population growth (from 6 to 7.5 billion in 2020), there is also an increased food demand as diets change with increasing economic

development of large sections of the population, and which was predicted to result in a grain gap of 13 million tonnes by 2010 (IFPRI 2001, McMichael AJ 2001) but this has increased more rapidly than anyone could have expected (Brown 2006). At the same time, and now predictable, have been the epidemics of chronic diseases and their outcomes (Darnton-Hill, Nishida, James 2004). So, while there is an absolute increase needed already, there will be conflicting needs of small farmers, national needs and those of the international markets (Webb 2003, Chopra & Darnton-Hill 2006). Some parts of the world, such as sub-Saharan Africa, are already disproportionately negatively affected (SCN 2001, Chopra & Darnton-Hill 2006). The Millennium Development Goals, seen as more likely to be successful, as agreed to by the richest countries in the world and by political leaders rather than health or nutrition sectors, is not showing a great deal of promise at present of reaching its targets, either in achievements, or in the realization of funding promises by these same countries (Keith 2005, Labonte, Schrecker, Sen Gupta 2005). For example, 33 countries, with a quarter (26%) of the world's population, are failing on more than half of all the targets. Looking at it from a more positive perspective, one could note that 55 countries, with 23% of the world's people, are on track to achieve as many as three-quarters of the Millennium Development Goals (UNDP 2002).

4.4 Re-positioning micronutrients

As noted above, despite all these truly well-intentioned declarations, the problem of malnutrition, especially protein-energy malnutrition, just seemed to get worse. Consequently, governments, including those who were donors, were increasingly more receptive to a possibly more manageable malnutrition problem. It was the vision of some of the global leaders in nutrition who were able to do this by reinventing (or as would be said in the advertising world, re-positioning) several of the vitamins and minerals- which, amongst other things became 'micronutrients'. This was most successful in the case of iodine, and then vitamin A, does not seemed to have happened with iron deficiency anaemia (for reasons that will be briefly discussed later), and seems to be happening with zinc and perhaps folate and vitamin B12. A further development of this trend is increasing attention to a public health approach with multiple micronutrients on the assumption that single vitamin deficiencies occur relatively rarely in populations consuming a poor diet with high infectious disease loads (Huffman et al. 1998) (with iodine being one example of where it can happen).

The World Bank specifically addressed the attraction of investing in nutrition as it was considered that it 'concretely improves the well-being of populations even when incomes remain low, and it offers the promise of increasing future incomes by boosting productivity. Investment in nutrition can help workers produce more and children learn more in school.' (Miller Del Rosso 1992). Increased involvement of the World Bank was seen as the firmest foundation for nutrition interventions in economic and social development (Prah Ruger 2005). This was seen as even more specifically so, for micronutrient interventions, which were predicted by the World Bank to increase the GDP by 3% while requiring an investment of only 0.5% of GDP (McGuire & Galloway 1994). Part of the more recent positioning has been the large role of vitamin A and iron deficiencies in the Global burden of disease reports of WHO and the World Bank (Murray & Lopez 1996). The then Director-General of WHO noted in an address to the WHA in 2003 that iron deficiency is amongst the ten leading causes of disease (Brundtland 2002). This has also helped to demonstrate the benefits of vitamin A and iron deficiency anaemia as affordable and cost-effective interventions (Sachs 2001), although even earlier reports were advocating for the cost-effectiveness of micronutrient interventions (Levin et al. 1993).

As noted, micronutrients received enhanced attention partly because of the relative failure to address protein-energy malnutrition and partly because of their perceived simplicity in developing intervention programmes. However, this still needed the micronutrients to be 're-positioned'. Why were these three selected? Clearly their prevalence had a lot to do with it, but even here, some repositioning was necessary.

4.4.1 Vitamin A

The identification of this deficiency had long been recognized in Asia (Oomen 1963) and was earlier a problem in Europe even into the early years of last century (Oomen 1976, Semba 2001b). Having often fallen in the gap between the perceived responsibilities of nutritionists and ophthalmologists, Sommer from Johns Hopkins University with Indonesian and HKI colleagues, observed that children supplemented with high-dose vitamin A had dramatically lower rates of mortality from infectious disease (Sommer et al. 1983). Although it was known since 1930s to have anti-infective properties, the declining prevalence in Europe and the US, and the more dramatic forms of eye disease

seen (xerophthalmia), had allowed this aspect of vitamin A to be largely forgotten (Semba 1999). The risk of blinding malnutrition, as it was sometimes called, was affecting maybe half a million children per year, a preventable tragedy but not one that caught the attention of health policy-makers in countries only able to spend less than a $1 a day on health. An Australian group, Glasziou and Mackerras (1993) did a meta-analysis of vitamin A interventions and found almost a quarter of children in endemic areas would be saved from infectious disease. A meta-analysis at about the same time, by Beaton et al. (1993) demonstrated a similar figure of 23% in deficient populations.

By demonstrating that vitamin deficiency was an important factor in child mortality, as well as blindness, vitamin A then became an international goal. This was reinforced when intervention trials showed significant success. A further likely factor is the relative ease with which vitamin A programmes could be monitored and reported on- partly because donors and governments can count and cost vitamin A capsules delivered twice a year when monitoring (although this is a lot harder to do accurately than might be imagined from the internal UNICEF tracking experience). The addition of vitamin A capsules to the polio national immunization days (NIDs) allowed coverage of over 85% in some of the poorest countries in the world (UNICEF 1998b, Mason et al. 2001, Aguayo et al. 2005). The impact has not been accurately assessed but UNICEF estimates something like 1.5 million lives saved over the last decade. Over 70 countries now have vitamin A programmes and/or policies- these figures are updated in chapter five (Dalmiya, Palmer, Darnton-Hill 2006). Vitamin A supplementation is a cornerstone of these interventions and this strategy should strengthen countries' ability and commitment, along with international and other partners, to make further progress towards the goal of the elimination of vitamin A deficiency as a public health problem by the end of this current decade (2001-2010).

Vitamin A deficiency has thus been redefined as a threat to early childhood survival, apart from its devastating contribution to childhood blindness. Hence interventions, from a government's perspective, immediately became more cost effective. Based on such experiences new approaches were also being redefined (Bloem, de Pee, Darnton-Hill 1998). The potential attractiveness to countries and donors increased again when West and co-workers reported from Nepal that β-carotene or vitamin A supplementation lowered maternal mortality (West et al. 1999). With the publication of the evidence base

for Child survival interventions, including vitamin A supplementation, and the strong support of the Canadian Government, vitamin A supplementation as an important intervention seems secure for some years yet (Black et al. 2003, Dalmiya, Palmer, Darnton-Hill 2006, West & Darnton-Hill 2007).

4.4.2 Iodine

Iodine deficiency was redefined (largely through the efforts of the ICCIDD) in a way that brought it to the renewed attention of the World Health Assembly, WHO Regional Meetings, UNICEF and Bilateral Agencies (especially the Canadian and Australian) and governments (Hetzel et al. 2004). Iodine deficiency had long been known as a problem throughout much of the world, although there was some complacency as salt iodization had been in place in much of the industrialized world for almost 50 years at that time. More importantly, up until the pioneering work of Hetzel, Pharaoh and others in the Highlands of Papua New Guinea in the 1960s and 70s (Hetzel & Pandav 1987), iodine deficiency was seen as the cause of goitre and cretins- goitre being a medical problem (usually surgically corrected in the industrialized countries). Photos of bizarrely large pathological examples on women and men from PNG, Africa and other exotic places, or as cretins, again generally in the same exotic places, as well as China and Himalayas, and even in quaint historical art works (e.g. a well-known Madonna and Child) in Europe (Hetzel et al. 2004) perhaps led to it being considered so exotic that it was less high on the international health and nutrition agendas. It may also have been a consideration that it was considered to have been largely solved in affluent countries.

What people like Hetzel and others did was to redefine iodine deficiency to become the 'Iodine Deficiency Disorders' (IDD) by showing that infants born to mothers living in endemic areas were likely to be neuro-intellectually affected, even if not clinically a cretin (Hetzel 1983), and even if mothers were not demonstrating clinically obvious goitres. When expressed in public health advocacy terms the estimated 10-15 points lost to infants born in iodine-deficient populations (Bleichrodt & Born 1994) and when multiplied by the number of births, the massive number of apparently lost IQ points to a nation was very convincing to policy makers (van der Haar 1997). There has been some work, but limited, to convert this into cost data and what this means in terms of economic losses (Hetzel & Pandav 1997, Sachs 2001, Andersson et al. 2005) and more recently in terms of the global burden of disease. From a redefinition from goitre to a continuum of iodine

deficiency disorders, and so vastly increasing the numbers at risk, especially for unborn children (WHO/UNICEF/ICCIDD 1993), this revised approach needed advocacy to compete with other priorities on the international agenda.

To do this, the International Council for Control of the Iodine Deficiency Disorders (ICCIDD) was formed and became extremely effective, particularly by clever use of the WHA process. From then to becoming one of the micronutrient goals of the World Summit and later the 1992 FAO/WHO International Conference on Nutrition in Rome, IDD has remained a priority. And with enormous success. When taken up by UNICEF and NGOs such as PAMM, MI and with massive funding by the Kiwanis, and subsequently the Gates Foundation to UNICEF, less than 20% of affected households were using iodized salt. Now over 70% of households in affected countries are covered by iodized salt (MI/UNICEF 2003, UNICEF 2007). Ironically, the European Region of WHO has one of the lowest coverage of iodized salt, partly through complacency but more importantly because of the emergence of countries from the Soviet system especially in Eastern Europe and the Central Asian Republics (Timmer 2004, Andersson et al. in press). The redefinition to a public health problem whereby even living in iodine-deficient environments was likely to affect normal brain development in whole populations, made the deficiency a lot more pressing problem. The possibility of a proven cost effective intervention, salt iodization, was a facilitating factor, but needed a partnership of governments, the United Nations Agencies, and private or parastatal salt mills. The spectacular success of the universal salt iodization process will be seen in chapter five, showing global trends. However, a challenge was the fact that the UNGASS 'World Fit for Children' goal of elimination of IDD was to be achieved by the end of 2005, which clearly did not happen. Good progress has been made, particularly over the last decade (Mangasaryan, personal communication based on most recent MICS findings from UNICEF and DHS findings, 2007 but not published at time of writing)

4.4.3 Iron

This remains the micronutrient in which least progress has been made. Iron deficiency anaemia (IDA) has not been so re-defined and has been over-medicalized and consequently is the only one of the three which has not shown real progress. The scientific iron community need to take some responsibility, consistently presenting a complex, medicalized view to public health national practitioners and policy makers, and

appearing to refuse to offer the compromises needed to get national programmes off the ground and funded. There is now an increasing emphasis to concentrate on the economic benefits of addressing iron deficiency anaemia and the proven effects on productivity (Aldermann & Horton 2007). This may be the re-definition needed, as the effect of even iron deficiency, i.e. before anaemia becomes apparent, on productivity is now well-established (Scholz et al. 1997, Haas & Brownlie 2001), as are estimates, using the 'Profiles' software, of just how many millions of dollars this is costing governments. Haas & Brownlie (2001) have concluded that the evidence is sufficiently strong to 'justify interventions to improve iron status as a means of enhancing human capital'. Further work by Ross and Horton (MI 1998) and Aldermann and Horton (2007) has strengthened these estimates to such countries, and has also demonstrated the impact on women and children (Darnton-Hill et al. 2005a).

The other challenge has been to try and simplify dosage regimes (e.g. 1-2 times per week compared with daily (Viteri 1998, Beaton & McCabe 1999, Stoltzfus 2001b, Cavalli-Sforza et al. 2005) and other ways to improve compliance, including improved supplies and logistics. More emphasis on the likely permanent neuro-intellectual damage of infants with sustained deficiency (Pollitt 2001, Lozoff et al. 2006), and addressing this as the last unresolved major (of the three) micronutrient deficiency may help. It was however not included in the mid-decade goals and was not initially included in UNGASS micronutrient goals. However there now appears to be a new emphasis for iron and some new lobby groups (e.g. IDPAS of the International Nutrition Foundation and funded by the MI) and fortification groups such as the Flour Fortification Initiative (FFI) and the Global Alliance for Improved Nutrition (GAIN). INACG never had the same influence as IVACG. However, clear funding sources of the magnitude of those for IDD and VAD are not forthcoming, although it did look as though the World Bank would take this on in the 1990s but it never really happened. The numbers affected should be persuasive enough but maybe this disease also needs further redefinition as a deficiency disease that affects the economic well-being and productivity of whole countries (MI 1998, MI/UNICEF 2003).

Other suggested factors are: iron interventions have proven to be programmatically difficult to do; have received less attention- partly perhaps because it mainly affects women and children; and, importantly, there has been a lack of consensus on treatment

and prevention (Stoltzfus 2001, Darnton-Hill, Paragas, Cavalli-Sforza 2007). There have been some encouraging steps in this direction with the publication of a consensus document by UNU/UNICEF/WHO/MI (1999) but with active participation of other partners, including NGOs and WHO (2001a). Just preceding that was a publication by Stoltzfus and Dreyfus (INACG 1998), and that with on-going work from IDPAS, have provided helpful programmatic advice (INACG 1998, IDPAS 2003). Nevertheless, the relative lack of progress will be seen in chapter five.

4.4.4 Multimicronutrients

In the meantime, folate and zinc are pushing their way on to the international agenda. Folate with possibly more acceptance at this point because of more interest to the affluent countries and the feasibility of flour fortification with iron and folic acid and other B vitamins (FFI 2005), although the treatment of diarrhoea with zinc, as well as oral rehydration therapy is now firmly established (WHO/UNICEF 2004b). With very low birth rates in many affluent countries, each infant gets more attention and resources, including the imperative to be protected from some of the relatively uncommon, but devastating neural tube defects that folic acid can help prevent. There is also now the probable link with homocysteine and heart disease in a world where chronic diseases are now the main global causes of adult death (WHO 1999b, Darnton-Hill, Nishida, James 2004). As noted earlier, there is now an international consultative group and meeting for zinc as a public health preventive option for children in developing countries, with increasing international acceptance (www.zinc-health.org), although while currently recognized by WHO/UNICEF (2004b) only as a treatment for diarrhoea, there is a strong push for zinc supplementation to also be considered as a preventive intervention.

Recognizing that those who suffer from any of the above deficiencies often suffer from poor diet and health in general, as well as other vitamins and mineral deficiencies, has renewed interest in food-based approaches, and in delivering multi-micronutrient supplements when necessary (Huffman et al. 1998, UNICEF/WHO/UNU 1999, SCN/WHO/UNICEF 2006). There has been recent re-interpretation of multimicronutrient formulations, as affordable interventions for the prevention of low birthweight, and maybe as a way of reducing progression to AIDS (Friis et al. 2004a, Fawzi et al. 2004) and as a public health intervention to reduce the incidence of low birthweight infants (SCN/WHO/UNICEF 2006). UNICEF, with WHO, has recently had several meetings to

address the public health nutrition community's position and to make recommendations on the use of multimicronutrients, including in emergency situations. This has been driven by a number of partners, including NGOs. A meeting convened by UNICEF with WHO, UNU and MI, of people experienced in micronutrient malnutrition control and prevention, came to agreement on a recommended composition for a multimicronutrient supplement for pregnant women for UNICEF and that has been used in both efficacy and effectiveness trials in at least nine countries on several continents (UNICEF/WHO/UNU 1999, SCN/WHO/UNICEF 2006). Universities, mainly from the UK, especially the University of Southampton, USA and the Netherlands, with national Universities and Institutes, and International NGOs such as Helen Keller International have been involved as partners in testing the effectiveness of such approaches in several countries in the region. Despite the intuitive, and public health, attractiveness of this idea, the idea of a multi-micronutrient supplement to poor women, even with one RDA of each component micronutrient, has met considerable opposition from USAID, and some academics, who claim it is unproven. From this writer's perspective it is almost unethical to withhold moving ahead on this, especially when e.g. upto 30% of the US population, already replete, take a daily vitamin supplement (Bender 2002), as do half of female US physicians on an irregular basis, with 35.5% on a regular basis (Frank, Benedict, Dennison et al. 2000) and over 70% of pregnant women (as is the USA recommendation). Stimulated by the recent research, and most recently the needs of the victims of the South Asian Tsunami, multimicronutrient supplementation is likely to move forward quickly. There is now a WHO/WFP/UNICEF statement recommending multimicronutrient supplementation to women, infants and children in emergency situations (WHO/WFP/UNICEF 2006). It is noteworthy that this has happened even without a specific goal.

4.5 Conclusion

Having re-positioned micronutrients, and established efficacy, there has been an on-going effort ever since to demonstrate broad effectiveness and cost effectiveness and cost-benefit (Sanghvi et al. 2007, Aldermann & Horton 2007). As Sanghvi et al. (2007) point out in their background papers to a proposed 10-year strategy for vitamin and mineral deficiencies prevention and control, there is enough evidence now to state that micronutrient fortification and supplementation are among the most cost-effective public health interventions available. However, they also note that there is enormous variation

in the documented costs of micronutrient programmes which vary greatly by specific cost measure, programme, type of intervention and delivery system, country circumstances and a range of other factors (Sanghvi et al 2007). This is further examined in chapter six.

Nevertheless, despite much progress, neither iodine nor vitamin A, and certainly not iron, actually achieved either the end of the 1990 decade goals or the 2005 goal for iodine, despite much success towards the goals in many individual countries, for at least the former two micronutrients. The subsequent (for the decade 2000-2010) micronutrient goal, emerging after a lot of pre-UNGASS discussion, and adopted by the UN as part of a special agenda on the child, has a different emphasis from the earlier one in that it mentions mechanisms. As noted, the 1990 World Summit for Children and the FAO/WHO International Conference in Nutrition in 1992 both called for the virtual elimination of IDD and VAD by the year 2000. But with relatively few countries having achieved these goals, "A World Fit for Children" (developed in preparation for the United Nations Special Session on Children in May 2002) effectively extended the time period to: "[a]*chieve sustainable elimination of iodine deficiency disorders by 2005 and vitamin A deficiency by 2010; reduce by one third the prevalence of anemia, including iron deficiency, by 2010; and accelerate progress towards reduction of other micronutrient deficiencies, through dietary diversification, food fortification and supplementation"* (UN 2002a). Progress towards these sub-goals will be addressed in the next chapter.

Chapter Five

5.1 Background

As noted in the previous chapter, there have been at least three important iterations of goals for micronutrients. Firstly, the various permutations of the original goals endorsed at the UN Summit for Children in 1900, including new emphasis on micronutrient interventions at the 'Ending Hidden Hunger' Conference in Montreal in 1991, and re-enforced at the FAO/WHO International Conference on Nutrition in Rome in 1992. Secondly, the more limited UNICEF/WHO mid-decade goals. Thirdly, the new goal at the UN General Assembly Special Session (UNGASS) on Children (known within UNICEF as the 'World Fit for Children' (WFFC) goals) in 2002 (UNICEF 2002). More recently, the Millennium Development Goals (MDGs), endorsed at the United Nations in 2000, have become the prime goals and targets for most multilateral and bilateral agencies and for many countries (UN 2000). While these address broad impact goals, such as alleviation of hunger and reduction of child mortality, micronutrient prevention and control activities are not explicitly mentioned at all and none of the indicators is a micronutrient indicator. Nevertheless, it has been argued that success in meeting the existing micronutrient goals are integral to virtually all of the MDGs, some more directly than others (SCN 2004). These goals, and their implications for micronutrient malnutrition, will be discussed further in Chapter 7.

Globally, although there has been tremendous progress with iodine and vitamin A interventions, micronutrient malnutrition remains a problem of public health significance in many countries. The last four decades have seen a period of rapid social and economic changes in most of the countries affected by micronutrient deficiencies. As reflected by shifts in under five mortality rates (U5MR captures the effects of nutrition, disease and social environments), the health and nutrition situation of the regions of the world can be reflected as: notable improvements in much of East Asia and parts of South East Asia; moderate progress in Latin America and the Caribbean; some progress in the Middle East; and a little improvement or worsening in child survival in much of sub-Saharan Africa (SCN 2004, UNICEF 2004b, UNICEF 2006a). These regional variations however mask marked inequalities. Undernutrition levels have improved only

moderately over the last 25 years, and much of this shift has been in one country, China. China's reduction of both undernutrition and U5MR has incurred a big environmental and social cost. There is certainly no inevitability towards greater economic security as seen in the late 1990s in South East Asia's financial meltdown and in countries such as Mongolia and Papua New Guinea and much of Sub-Saharan Africa, and to a lesser extent, Eastern Europe and Central Asia, all of which have seen negative shifts in many economic, social, and nutrition and health indicators. Even the USA is running the greatest national financial deficit in history.

Emergency situations, both acute and chronic, increasing global insecurity, and globalization are all having an impact on the health and welfare of peoples. UNICEF resources spent on emergencies, both environmental and civil, have increased to over 20% of the total expenditure over the last decade. At the national level, except in much of sub-Saharan Africa and some South-East Asian countries, most countries do not have a national food security problem, but problems of household food security and dietary deficit and individual malnutrition are still common among low income populations (SCN 2004). Social inequalities in nutrition and inequities in health experience persist everywhere (Darnton-Hill & Coyne 1998, UNDP 2003, UNICEF 2006b), and for those currently malnourished populations, the overall nutritional picture, especially of undernutrition, does not promise to improve much over the next 20 years (Darnton-Hill & Coyne 1998, Smith & Haddad 2000, SCN 2004) without a much increased rate in the change of existing patterns (UNICEF 2006a). The 2005 World Health report noted that 'numerous women and children are excluded from even the most basic health benefits; those that are important for mere survival' (WHO 2005). Some countries, often the poorest, show a pattern of massive deprivation, with only a small minority, usually the urban rich, enjoying reasonable access to health care, while an overwhelming majority is excluded. Among those left out, women and their children suffer most (WHO 2005a).

In this chapter, the subject is solely the specific micronutrient goals, although it is recognized that achieving the micronutrient goals will be an essential contribution towards the MDGs by increasing nations' intellectual capacity and economic productivity, and by reducing infectious disease levels and infant and young child and maternal mortality (SCN 2004). At the same time, the achievement of many of these MDG goals e.g. an increase in female education, reduction of global levels of malnutrition, halving of

poverty levels, would also have an impact on micronutrient status as part of improved nutrition and health.

The information in this chapter is drawn from a variety of referenced, but diverse, sources including from databases of WHO and UNICEF and organizations such as Macro International (USAID), ICCIDD, IDPAS, MI, University of Tulane, and so on. Much of the data compilation was developed during the course of an advocacy initiative by UNICEF by the author, with considerable technical help from the University of Tulane (Mason et al. 2004), and draws heavily on that and their earlier work (Sethuraman et al. 1997, Mason et al. 2001) and which also was largely the basis for the Vitamin and Mineral Deficiency Report (MI/UNICEF 2003). Also used are more recent updates during the development of internal UNICEF strategies for vitamin A and the iodine deficiency disorders. DevInfo, developed by the UN System from the earlier UNICEF ChildInfo, was accessed for information on human development and relevant health and nutrition indices (http://ww.devinfo.org). Of the eleven nutrition indicators, only two relate directly to micronutrients: vitamin A supplementation coverage and proportion of households consuming iodized salt. There is notably not one for iron deficiency or anaemia, although the DHS does collect these data in many countries. A review for the Ten Year VMD (Vitamin & Mineral Deficiencies) Strategy consolidated much of the current data (Borwankar, Sanghvi, and Houston 2007). Macro International Inc. also issued a 'Micronutrient Update' based on DHS data in January 2007 (Mukuria & Kothari 2007). More recent data will be available at the end of this year (2007) from the updated MICS (UNICEF Multiple Cluster Surveys) and USAID's Demographic Health Surveys (DHS). Preliminary analysis (some of which became available for vitamin A and iodine) is apparently suggesting increased progress in the prevention and control of micronutrient deficiencies. This chapter does not specifically address the progress towards the MDGs, beyond noting that to be achieved there will need to be a global acceleration of effort. They will also be discussed more in Chapter 7.

The first section reviews monitoring and evaluation, which has generally been inadequate, especially in terms of being able to identify trends accurately, or even programmatic 'lessons-learned' (Mannar & Mason 2004, Mason et al. 2004a,b, Borwankar, Sanghvi, Houston 2007), then a review of four periods: (i) 1990 and before; (ii) data and trends up to 2000; (iii) projected trends up to 2010; and, (iv) the current

decade 2000 to 2010 but with the most recent data generally coming from 2005. This leads into the next chapter (Chapter Six) identifying lessons learned, constraints and facilitating factors.

Monitoring and evaluation

One of the advantages of establishing goals is the increased likelihood of activities and outcomes being more rigorously monitored by countries, often to fulfill requirements of the donors, but also to provide information for a series of global databases being managed by different institutions. The needs for information have taken three, somewhat overlapping forms: monitoring, surveillance and evaluation. The first steps of assessment to identify and quantify the problem have, in the majority of countries, already taken place, although it has been noted that 'most countries implement national programs without up-to-date (within the previous five years), nationally representative, population-level biochemical, clinical, or functional deficiency data' (Deitchler et al. 2004). A recent review pointed out that apart from vitamin A, iodine, iron and anaemia, data on prevalence of micronutrients are weak and surveys are needed to fill those gaps and that there is a need for developing, field testing and applying field methods for other micronutrients (Borwankar, Sanghvi, Houston 2007). The present indicators have considerable limitations: biological indicators are more specific but they are also more often invasive, cumbersome and expensive, whereas functional indicators are usually less sensitive and less specific.

5.1.1 Monitoring

Monitoring is used here in the sense of repeated examination of programmes devoted, in this case, to micronutrient malnutrition prevention and control. This is more often at the local, national and regional level and generally uses process indicators e.g. vitamin A capsule coverage. From a local or national perspective this is often a tool to be used in logistics and for ensuring adequate supplies (supplements, iodized salt, iron/folic acid tablets etc.) for national campaigns and for local health centre use. The mid-decade goals were also essentially process indicators and were used to assess progress and to identify intensified action as needed (UNICEF/WHO JCHP 1994a, b). Such monitoring also can help to satisfy donor needs e.g. USAID's 'intermediate goals' requirements in project reports to show some progress when too early to demonstrate impact. UNICEF

annually expends considerable effort monitoring both the assessed vitamin A capsule national needs and then the implementation of the programmes it supports. To monitor necessary steps to achieve sustainability in iodized salt programmes, a matrix has been developed by the ICCIDD and its partners (and adapted by UNICEF at the initial instigation of the author) that shows the impact of IDD programmes in countries by urinary iodine levels and iodized salt coverage and uses as a monitoring system the ten process indicators agreed to by WHO and partners (WHO/UNICEF/ICCIDD 1999, 2001), now consolidated to seven (Untoro, personal communication 2007). More regular, focussed monitoring would be expected to promote stronger programmes and allow trends to be established. They must, however, also provide useful information to implementers at all levels, including at Village Clinics and Community and District Health Centres, or for use in outreach programmes. They should also be realistically included in initial budgets by donors and governments.

Two important sources of monitoring information at the global level are the USAID Demographic Health Surveys (DHS) and the UNICEF Multiple Information Surveys (MICS). They intentionally complement one another and are valuable, often the only, sources of national information. For micronutrients, the WHO databases (partially funded by UNICEF) are essential and rely on Government-provided information that is then rigorously confirmed and is now available for vitamin A, iodine and iron (www.who.int). It is not always possible to get nation-wide information and then a series of pre-defined definitions are used to identify which sub-national data will be included. Other sources include national Government data, research data from Universities and other institutions, such as the US Centers of Disease and Prevention (CDC), and NGO data, especially as compiled by the Micronutrient Initiative (www.micronutrient.org).

5.1.2 Surveillance

Effectively surveillance is on-going monitoring, but includes bio-medical outcomes e.g. levels of night-blindness that can be expected to change after a supplementation round with vitamin A capsules. The DHS surveys also sometimes include bio-medical outcomes, such as haemoglobin levels. Surveillance helps to pinpoint distribution and supply problems and to identify hard-to-reach populations that are being missed. Repeated cluster sampling has been used, as well as sentinel sampling. One of the

most impressive is the surveillance system of the INGO (PVO), Helen Keller International in Bangladesh, and later Indonesia (HKI 2000). This has also been used to detect changes in the prevalence of micronutrient deficiencies in times of crisis, and incidentally to identify micronutrient deficiencies of vitamin A and iron as sensitive early indicators of emerging nutritional stress (Bloem & Darnton-Hill 2001, HKI 2000, Block et al. 2002, Bloem, de Pee, Darnton-Hill, 2005). The DHS surveys, when repeated, act in this role of showing change over time although are not generally designed for this, and cannot be used at district level to show change in most cases (Sharman 1998). As noted above, complementing the DHS information have been the UNICEF MICS surveys, which are also used in the annual UNICEF State of the World's Children Reports, as well as in periodic updates such as progress during the decade 1990–2000 in preparation for the UNGASS for Children. The latest surveys are now being used in an evaluation of progress towards the World Fit for Children goals (due late in 2007) and updated reports in the meantime (UNICEF 2004, 2006) - the 2006 report was specifically focused on nutrition. Unfortunately, some of the data collected by both systems have not been able to be analyzed due to lack of resources. As noted the information from the new round of MICS and DHS will not become available until the end of the year and so were unavailable at the time of writing.

A consortium of national health information systems (HIS) and international agencies, coordinated by FAO has tried to institute FIVIMS (Food Insecurity and Vulnerability Information and Mapping Systems) that could and has been used for micronutrient status surveillance (FAO 2005), but has not been widely adopted. Likewise, in a slightly longer framework the VMNIS (Vitamin and Mineral Nutrition Information System - previously MDIS or Micronutrient Deficiencies Information System) of WHO has monitored progress over the decade but has faced challenges because of different methods used in each country, and changing norms e.g. moving from goitre to urinary iodine levels, and because many studies are sub-national (WHO/UNICEF/ICCIDD 1993, WHO/UNICEF 1995, WHO 2004). They have largely overcome this by rigorously defining how data will be used, and when to be included and defining study criteria being supplied by the national, or sub-national, data (WHO 2004, Andersson et al. 2005). However, this makes the identification of trends over time very difficult to establish. The use of websites showing data by various partners has been a useful development over the last decade including those of the UN Agencies, ICCIDD, the Micronutrient initiative,

IDPAS (Iron Deficiency Program Assistance Support) through the International Nutrition Foundation and UNU at Tufts University, and others.

5.1.3 Evaluation

Evaluation is defined as meaning the identification of success, or failure, in reaching previously agreed-to targets and objectives, and measures the impact of a particular intervention or set of interventions. It has been done at two levels. Firstly, at a project level at the end of a specified funding cycle, or conclusion at a previously agreed-to evaluation time; and, secondly, at a national and global level to assess success at country level, for example the indicators being used to show that a country has achieved IDD elimination success (WHO/UNICEF/ICCIDD 2001). UNICEF tackled this most aggressively in the lead up to the UNGASS to show progress over the preceding decade, identify constraints/challenges and to help in the setting of new goals using the MICS (UNICEF 2001). The University of Tulane with UNICEF and the Micronutrient Initiative, have systematically done this for the three main micronutrients (Mason et al. 2001) and parts of this are now on various websites, such as www.micronutrients.org. It is this work that has been recently updated and is the source of much of the current data on trends (Helwig, Rivers, Mason 2004, Mason, Rivers, and Helwig 2005). Unfortunately, as noted, for even more recent data that are already apparently showing positive changes, the results of the 50 or so new MICS and DHS will not be out until the end of 2007 (and hence not available for this chapter). However, much work has been done by WHO in updating their sites for vitamin A deficiency, iodine deficiency disorders and anaemia prevalence (www.who.org) and by UNICEF for vitamin A supplementation coverage (Dalmiya, Palmer, Greig 2006, UNICEF 2007) and iodine deficiency (Mangasaryan et al. 2005, Untoro 2007, unpublished).

UNICEF has the responsibility for maintaining coverage data, for example on coverage of vitamin supplementation and use of iodized salt in households, and also on underweight, amongst many other indicators, usually with other partners, such as WHO, which keep databases on prevalence, MI and IDPAS on programmes; and for fortification, GAIN and FFI. In the last two years, GAIN has coordinated a working group of the VMD (Vitamin & Mineral Deficiencies) 10-year strategy process, led by MI and WHO to help with coordination and harmonization of micronutrient data. An early effort to get more accurate data on coverage was done with the Government of

Bangladesh, HKI and UNICEF in Bangladesh in late 1980s to try to distinguish between the institutional information on coverage by government of vitamin A capsules (often recorded as over 100%) and the suspected reality, which turned out to be around 34%, and also to identify logistical and performance blockages (Darnton-Hill et al. 1988). The Previous MOST Project of USAID has more recently commissioned such work, effectively using the process to develop new interventions to follow the phase moving beyond the Polio National Immunization days (Houston 2003, Rassas et al. 2003, Rassas et al. 2004). A more recent study of 21 countries by UNICEF and MI identified programmatic blocks and also functioned as an evaluation of the effectiveness of vitamin A supplementation programmes in these countries (MI/UNICEF, in preparation). An even more ambitious project by MI, University of Tulane, CDC and UNICEF undertook a research study of country experiences in micronutrient deficiency control from 2000 to 2002 with University and research partners in-country, which focussed on South and South East Asia plus South Africa (Deitchler et al. 2004, Mason et al. 2004a,b). This last will be particularly referred to for 1990-2000, although results were not always consistent with WHO databases, due to differing methodologies. WHO databases are subsequently being used for evaluation data. The results in this chapter are from all these sources, conference reports (e.g. IVACG) and other unpublished reports, and the two more recent UNICEF in-house updates.

The chapter examines trends and what these might mean in terms of reaching the various goals. Mason et al. (2001) have also suggested some implications of positive trends that are important programmatically: how to sustain success; how to generate permanent solutions; how to achieve full coverage by various means, and how to ensure useful monitoring and adequate quality control. These facilitating factors will be addressed in Chapter 6. Where the limited number of repeat surveys (8 in 1998) did not show a positive trend in their 2001 report (e.g. for vitamin A capsule coverage in Nigeria, and more surprisingly Nepal) then it becomes important to identify constraints and reasons why not, how to get further resources and how to sustain any subsequent progress. Often this boils down to how to develop and supplement effective, large scale programmes that are suited to the conditions and resources of poor countries.

The other important pre-requisite is to have some concept of what measures success. The obvious one, given the context here, is the attainment of the international goals.

This will be a major measure. However, few countries had, at the time of the earlier reports in 2001, achieved success by this measure. Therefore the measures fall back on a series of process measures e.g. policy, legislation, coverage of supplements, coverage by fortification, and even harder to measure, dietary adequacy. Being a nutritional intervention, micronutrient malnutrition needs to have some indicator of sustainability. Reaching the goal just once, or for a couple of years, cannot be considered a success in the longer term. Iodine deficiency is illustrative in this respect. Similarly, the previously used criterion of one capsule of vitamin A over the previous year, is no longer considered adequate, as it does not protect the child, and is now replaced by 'one capsule in the previous six months'. So far, more emphasis has been placed on evaluation (perhaps reflecting immediate donor needs) than on sustainability measures.

The best data are for iodine, vitamin A and iron deficiency (or usually anaemia). However, where improvements have been seen because of societal change, it is likely other aspects of the diet have also improved and hence the intakes of other micronutrients. Iodine deficiency disorders, as measured both by impact and process indicators have been reduced and the attempt at elimination, as will be seen, is thus a remarkable public health success (Andersson et al. 2005), as has been reduction of the more severe manifestations of vitamin A deficiency (xerophthalmia) (West 2002, Ahmed & Darnton-Hill 2004, West & Darnton-Hill 2001, 2007); whereas there has been virtually no discernable improvement on global levels of iron deficiency as measured by anaemia (Mason et al. 2001, McLean et al. 2007).

5.2 Baseline estimates at 1990 and before

There had been relatively little incentive to gather global prevalence data before the UN Micronutrient (and other) Goals were widely endorsed at the 1990 World Summit for Children (WSC) (UNICEF 1990) and then endorsed at the 1992 FAO/WHO International Conference on Nutrition (FAO/WHO 1992). Most of the work had been done by academic institutions and by WHO and FAO as the normative agencies of the UN and because they, and UNICEF, had to report to their Executive Boards and respond to World Health Assembly resolutions. Consequently, there was a concerted, if not entirely coordinated, effort to get data that could be used as baseline and which culminated in the WHO MDIS (Micronutrient Deficiencies Information System), usually

with UNICEF and other special interest partners such as IVACG for vitamin A, and ICCIDD for iodine (WHO/UNICEF/ICCIDD 1993, WHO/UNICEF 1995). Later, subsequent World Fit for Children (WFFC) goals in 2002, took the 1990 values as the baseline against which progress would be measured, and which was a continuing incentive. However, these 'baseline' values were somewhat unclear and were generally broad estimates and extrapolations.

The following brief outlines of prevalences of the three micronutrients at 1990 is shown to give both an idea of prevalence and also relative numbers at that time. This data comes mainly from early WHO reports and from the report prepared for UNICEF by the University of Tulane (Helwig, Rivers, Mason 2004). The latter used virtually the same data used in the Vitamin and Mineral Deficiency Report of 2003 (MI/UNICEF 2003).

5.2.1 Vitamin A

It was only in the late 1980s that it became accepted that vitamin A deficiency had a role in childhood deaths from infectious diseases (Sommer & West 1996). The role of vitamin A in the aetiology of preventable childhood blindness was however relatively well-known. Countries such as Bangladesh and India have had programmes in place since early 1970s, a national one in the case of Bangladesh (Darnton-Hill et al. 1989). However, there were relatively few data on prevalence available- mainly that of Oomen and colleagues and McLaren and colleagues for WHO (Oomen 1963, Oomen, McLaren, Escapini 1964, McLaren, Oomen, Escapini 1966). At these times, the interest was in the ophthalmic manifestations of vitamin A deficiency, and as these were relatively rare, required large population numbers to detect a public health problem as defined by WHO (Sommer 1992). An early impressive example was the Bangladesh national survey done by Cohen and colleagues for the Government through HKI (Cohen et al. 1985, IPHN/HKI 1987). Nevertheless, the global situation, as largely defined by xerophthalmia, could only be extrapolated from the WHO MDIS of 1995 (WHO/UNICEF 1995) and estimates of vitamin A deficiency varied considerably (West 2002). In 1987, WHO had estimated that vitamin A deficiency was endemic in 39 countries, mainly based on clinical eye signs but this was clearly an under-estimate (WHO 1995). By 1995, WHO was estimating a problem in 60 countries and a 'likely' problem in a further 13 (UNICEF now has 103 target countries for vitamin A supplementation). The source of the figures for 1990 are from estimates of WHO (WHO/UNICEF 1995) and of the

University of Tulane (Sethuranam et al. 1997, Mason et al. 2001). Vitamin A deficiency was estimated by the WHO Micronutrient Deficiencies information System (MDIS) as 254 million 'preschool children' (as countries had used differing age ranges in surveys) 'at risk' in terms of their health and survival (WHO/UNICEF 1995). An estimated 2.8 to 3 million of these were thought to be clinically affected. The estimate by the University of Tulane for 1990 was 7.4 million with xerophthalmia and 238.8 million vitamin A deficient - similar overall figures but over double the number estimated to have clinical xerophthalmia.

The preface of the WHO vitamin A MDIS report specifically notes one of the purposes as using the data to 'serve as a baseline for tracking progress nationally and globally towards the virtual elimination of VAD, which is one of the end-of-decade micronutrient goals…' (WHO/UNICEF 1995).

5.2.2 Iodine deficiency disorders

Although WHO had expressed concern about iodine deficiency as early as mid-1960s, it was not until (as described in Chapter 4) the condition was repositioned as the spectrum of iodine deficiency disorders in the mid-1980s, that it became a higher priority on the international health agenda. Nevertheless, WHO had published in 1960 the first global review on the extent of endemic goitre, covering 115 countries and started the focus on iodine deficiency as a global public health problem. While there were relatively few global data on the actual size of the problem before 1990, (the MDIS report was published in 1993 by WHO/UNICEF and ICCIDD), the ICCIDD had already formed at the ACC/SCN meeting in Nepal in the late 1980s (Hetzel 2005) at which time the need for better data to help address the new goal became apparent. This was despite voluntary salt iodization having been in place in the USA and parts of Switzerland since the 1940s. In 1990 the World Health Assembly passed the first of its resolutions on eliminating iodine deficiency and its disorders. In the 1993 report, the number of countries affected at that time was considered to be 110 (WHO JCHP 1993) and an estimated 12.0% of the total global population to have iodine deficiency as measured by TGR (total goitre rate now TGP or total goitre prevalence) (WHO/UNICEF/ICCIDD 1993). The estimate of the Tulane group was somewhat higher again at 17.6% of the global population (based on available prevalence data from 1992 to 1996) (Mason et al. 2004). An update of iodine

status has recently been published by WHO (in collaboration with UNICEF and ICCIDD) but it has been difficult to show trends due to a switch, for good diagnostic reasons, to urinary iodine excretion as the main indicator (WHO 2004). Mason has used modeling to show trends (Mason et al. 2005) using TGR to address this and overcome the apparent anomaly of the WHO trend, which is discussed later in this chapter.

5.2.3 Iron deficiency anaemia

Iron deficiency anaemia had been recognized as a medical problem for longer than the other two micronutrients, but even now lacks a good global prevalence figure, although 2 billion (2,000 million) is most frequently quoted (MI/UNICEF 2003). This prevalence figure has recently been updated by WHO in 2007 to just over 1.55 billion although the figures are not comparable because of very different methodologies (McLean et al. 2007). The likely earliest global prevalence estimates were from DeMaeyer and colleagues at WHO in late 1980s (DeMaeyer et al. 1989) with a heavy weighting of figures from small surveys, mainly from Europe and not at all representative of global population distribution (Deckelbaum, personal communication). The lack of agreement of the best measures and indicators to be used have frequently been an issue but in fact it is virtually always anaemia prevalence that has been used. The question being the degree to which anaemia reflects iron deficiency. A common estimation is that there will be the same number again iron deficient as those demonstrating iron deficiency anaemia (Yip, Stoltzfus, Simmons 1996, Stoltzfus & Dreyfus 1998, Yip 2002), but this clearly depends on other factors in the epidemiological environment such as malaria, and maybe helminth levels, and now HIV prevalence. Another factor is other causes of anaemia, both nutritional (folate, vitamin C, vitamin A, vitamin B12 deficiencies and protein-energy malnutrition) and non-nutritional (chronic disease such as TB and cancer, HIV/AIDS, malaria and so on) (Darnton-Hill, Paragas, Cavalli-Sforza 2007). Although WHO and CDC (Centers for Disease Control & Prevention) held a technical consultation to make recommendations on indicators (WHO/CDC 2005), some of the cut-off points remain uncertain e.g. for infants. The estimated prevalence before 1990, were basically those of DeMaeyer et al. at WHO (1989) which, when China is excluded from the latest WHO figures, were somewhat lower as group percentages of pre-school children, and pregnant and non-pregnant women, but cannot really be compared because of differences in methods and coverage (McLean et al. 2007) and more details of this will

be given below. By the University of Tulane estimations for 1990 non-pregnant women had a prevalence of 41.7% or 404 million women, 43.7% or 41.8 million pregnant women and 53.0% or 282.7 million preschool children (Mason et al. 2001).

5.2.4 The mid-decade goals

The above demonstration of a lack of good estimates before the early 1990s perhaps shows the marked impact of the goals in helping to increase focus on the magnitude of the problem, and the need to have some good measure of this to monitor and evaluate efforts to eliminate and reduce the micronutrient deficiencies. The adoption of international goals could also be argued to have accelerated a research effort that continues to be translated into country programmes (ACC/SCN 2001) and hence by the year 2000 there were reasonable estimates to act as a baseline of 1990, as both WSC and ICN goals stipulated, by working backwards. However, there were fewer indications of progress in the early part of the 1990-2000 decade. The mid-decade goals were specifically recognizing that, without an increased and sustained effort, the earlier World Summit for Children goals agreed-to in 1990 would not be reached in a majority of countries. The mid-decade goals were therefore designed and adopted by the UNICEF-WHO Joint Committee on Health Policy, to be implementable and achievable so at least some successes could be posted by the end of the decade (UNICEF/WHO JCHP 1994a, b). However, they suffered from the fact that they were generally vague and hence hard to evaluate e.g. adequate vitamin A from dietary sources. They also suffered, largely because of UNICEF pressure on country offices, because results were often stretched to fit the organizational need (this seems to have been particularly true of UNICEF and Baby Friendly Hospital Initiative) (personal observation 1995).

For each of the major three micronutrients, progress was measured by achievement of process goals, using these mid-decade goals, such as adequacy of vitamin A intake, adoption of USI and so on. There was no formal mid-decade goal established for iron, although there was a subsequent effort to create a mid-Decade Goal for iron but it did not really gel. The JCHP did subsequently agree that the goal on anaemia should be expanded to include reducing anaemia in children (Underwood 1994) but as it turned out, that would have to wait until new goals in 2002.

The two mid-decade micronutrient goals were to ensure:

- 'universal salt iodization in IDD-affected countries (90% or more of food-grade salt iodized or more than 90% of households consuming iodized salt)'
- 'that at least 80% of all children under 24 months of age living in areas with inadequate vitamin A intake receive adequate vitamin A through a combination of breast-feeding, dietary improvement, fortification and supplementation'

The wording was subsequently modified but still remained hard to monitor. Nevertheless, the goals certainly gave an impetus in the drive to reach the goals, but apparently not enough, as none of the three international end-of-decade goals was reached by the end of the year 2000. Of the three micronutrients being discussed, the elimination of the iodine deficiency disorders came closest (UNICEF 2001, Mason et al. 2001). The next section on measuring progress will show the best estimates of the situation at the end-decade point.

5.3 Progress at the end of the decade

The mid-decade goals probably did accelerate progress in many countries and certainly are likely to have helped document the salt iodization process, particularly by UNICEF (UNICEF 2001) and stimulated a review by WHO of progress, as measured by goitre rates for IDD (WHO/UNICEF/ICCIDD 1999). As noted, the vitamin A mid-decade goals were hard to measure accurately and the push for vitamin A programmes, especially supplementation, came more from a consensus meeting and statement at UNICEF in New York in 1999 to launch a Vitamin A Global Initiative (UNICEF/MI/WHO/CIDA/USAID undated). Towards the end of the decade, other micronutrients were being acknowledged to have public health significance e.g. folate and zinc, and the possible implication of multi-micronutrients on low birth weight was gaining priority, especially in UNICEF (Shrimpton 2003). Mason and colleagues in UNICEF and MI did important projections from the limited repeat data available on rate of progress towards the goals that fed into the work of UNICEF, with WHO and FAO, in developing the next set of goals (Sethuraman et al. 1997, Mason et al. 2001).

5.3.1 Vitamin A

Earlier estimates of vitamin A deficiency in pre-school children had ranged from 75 million (MI 1998) to 254 million (WHO/UNICEF 1995). A more recent estimate, almost certainly an underestimate as older children were not included, was approximately 127 million and 4.4 million pre-school children with vitamin A deficiency (serum retinol<0,70µmol/L) and xerophthalmia, respectively (West 2002). However, the expansion of vitamin A supplementation programmes was also not able to be factored in and coverage continues to increase (Dalmiya, Palmer, Darnton-Hill 2006). The same estimates from West (2002) gave 7.2 million pregnant women vitamin A-deficient (<0.7µmol/L) with another 13.5 million having low vitamin A status (0.70-1.05µmol/L). Over six million women develop night-blindness during pregnancy every year (West 2002). Experience with vitamin A and vitamin A deficiency (VAD) was however progressing in both Asian and Latin American regions, especially in virtually eliminating xerophthalmia as a public health problem, and in so doing, gaining national experiences that were then being transferred to other countries. Bangladesh, Indonesia, Philippines, and Viet Nam all saw national prevalences drop to below levels designated by WHO as constituting a public health problem although pockets of high prevalence continued to exist, particularly in poorer provinces. India, and now Nepal, have demonstrated a decline in prevalence, particularly of xerophthalmia (Sethuraman et al. 1997, Darnton-Hill 1998, Mason et al. 2001). It was estimated in 1995 that about 17 countries were 'on track' to reach the WSC goal. By 1997 there were already 30 such countries, reflecting the surge in activities at this time (Sethuranam et al. 1997, UNICEF/MI/WHO/CIDA/ USAID undated). This was at a time, as noted earlier, when activities to address undernutrition in general (i.e. non-micronutrient) were decelerating.

The different approaches that have been used in programmes towards the elimination of vitamin A deficiency (VAD) have included: food-based, such as dietary diversification through home gardening and nutrition education; fortification with vitamin A of sugar, flour, margarine and edible oils, noodles and condiments; and supplementation with high-dose capsules including through national distribution to all preschool children. The last have been through National Immunization Days (NIDs), and more recently through health system centres, with E.P.I. and other child survival interventions, and now increasingly through out-reach programmes such as Child Health Days and Weeks, and

post-partum supplementation (200,000 IU within 6-8 weeks of birth). Although 44 countries had reported adoption of policies by 2000 for supplementation of all mothers with high does vitamin A capsule within 8 weeks after childbirth, actual coverage by this method had been disappointing- at least partly because many mothers are delivered in situations where the post-partum vitamin A was not readily available, or mid-wives were not aware of the policy. A recent technical brief from the A2Z Project of USAID has recently evaluated the evidence for this intervention and concluded that more evidence is needed and more clear guidance from WHO (Rice 2007).

The highest prevalences of VAD continued to occur in South Asia and sub-Saharan Africa, where 30-40% of pre-school children continued to be at risk. By late 1990s about half of the countries in the developing world had adopted national policies for addressing VAD in general. In the countries having policies, and probably co-incidentally where most success has been seen, two thirds were in countries of the UNICEF Region of East Asia and the Pacific, and one third in the Middle East and Northern Africa. An unexpected problem was recognized early in the last decade (1990s) in the Micronesian island nations where these are becoming overcrowded and urbanized, such as Chuuk in the Federated States of Micronesia and in Kiribati. There appears to be a special risk for atoll islands with limited soil capacity and which already import a lot of food of doubtful nutritional value. These countries have now instituted a variety of vitamin A prevention and control programmes, including the promotion high β-carotene containing traditional varieties of banana (Englberger et al. 2003).

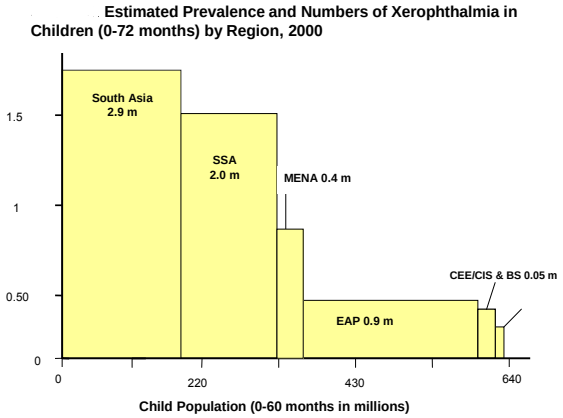
In most cases the main intervention has been with supplementation although fortification has been the major thrust in Central America, and home gardening interventions and social marketing approaches have been successful in Bangladesh and Indonesia, amongst others (HKI 2003b). By the end of the decade, forty-three (43) countries had supplementation programmes covering one round of over 70% and 13 had two rounds (the target now used as a measure for success) (UNICEF 2005). Some other countries should be included as successful in that they achieved their stated aim of a more targetted coverage of geographic areas considered highly at-risk areas as opposed to a nation-wide programme. As noted, a variety of measures have been used from routine delivery from health centres to major national campaigns, to out-reach with relatively unschooled volunteers. The national immunization days were spectacularly successful

especially in Africa and it was presumed it would be a real challenge to maintain such levels without them, although outreach or national Micronutrient or Child Health Days were already starting to work in many countries. In Nepal, supplementation has been consistently expanded through delivery by Female Community Health Volunteers, and has now been extended to all districts with coverage of 90% (Fiedler 2000). Indonesia had been able to show coverage, through health centres, of around 60%. These are important examples as more countries move towards decentralized health systems. India has had a long history of vitamin A supplementation through the Integrated Child Development Services programme which delivers vitamin A to children less than 5 years as part of its comprehensive activities since 1975, but appears to have had a relatively small effect on subclinical vitamin A deficiency (West & Darnton-Hill 2001).

To report on the previous decade to the UN, UNICEF published a report on progress since the World Summit for Children (UNICEF 2001) which estimated that about one million child deaths may have been prevented through vitamin A supplementation between 1998 and 2000 (UNICEF 2001). By the end of 1999, coverage with at least one round of vitamin A supplementation (not in itself adequate for protection) was 70% for Sub-Saharan Africa, 66% for East Asia and the Pacific (excluding China), only 35% for South Asia and 34% for Latin America and the Caribbean (UNICEF 2001). The statistical report noted that there was 80% coverage in the least developed countries (but which was something of an artefact caused by high success of the polio NIDs - at least initially the coverage of the second round was very low). Contrary to the UNICEF and WHO coverage data, those of Mason's group were higher and perhaps overly optimistic although they had sought more direct sources of data. Since 1994, they estimated that vitamin A supplementation in South Asia had increased from 52 to 75%, and in East Asia and the Pacific from 25% to 86% (Sethuraman et al. 1997). Of countries with a VAD problem, 83% (5/6) in South Asia had vitamin A supplementation policies and 89% (8/9), in East Asia and the Pacific, and for countries with populations of less than one million (as in much of the Pacific), 60% (Sethuraman et al. 1997).

The two bar charts (Figure 5.1) show the relative size of the problem by UNICEF Regions demonstrating the highest prevalence and numbers in South Asia, with Sub-Saharan Africa next (SSA). There was a lower prevalence in East Asia and Pacific

region (EAP), but still with large population numbers affected (Mason et al. 2004, Helwig, Rivers, Mason 2004).



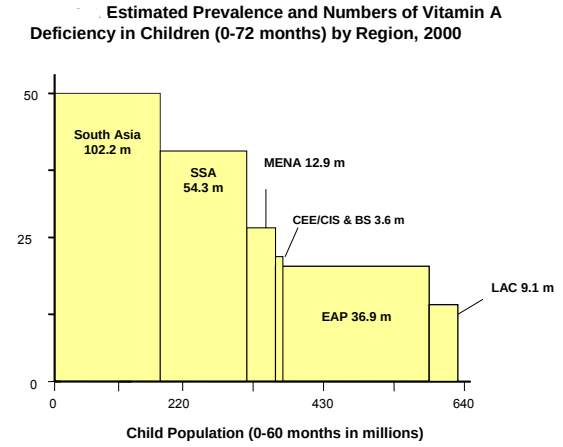


Figure 5.1 Estimated prevalence and numbers of xerophthalmic and vitamin A deficient pre-school children in 2000 by UNICEF region (Helwig, Rivers, Mason 2004)

The map below shows the geographic distribution of vitamin A deficiency (Figure 5.2) at that time but the map would not look much different today, at least in terms of the countries affected, although given the coverage with vitamin A supplementation in the later map (Figure 5.14), the prevalence of vitamin A deficiency will certainly be less in some countries.

Vitamin A Deficiency Prevalence (children 0-72 months), 2000

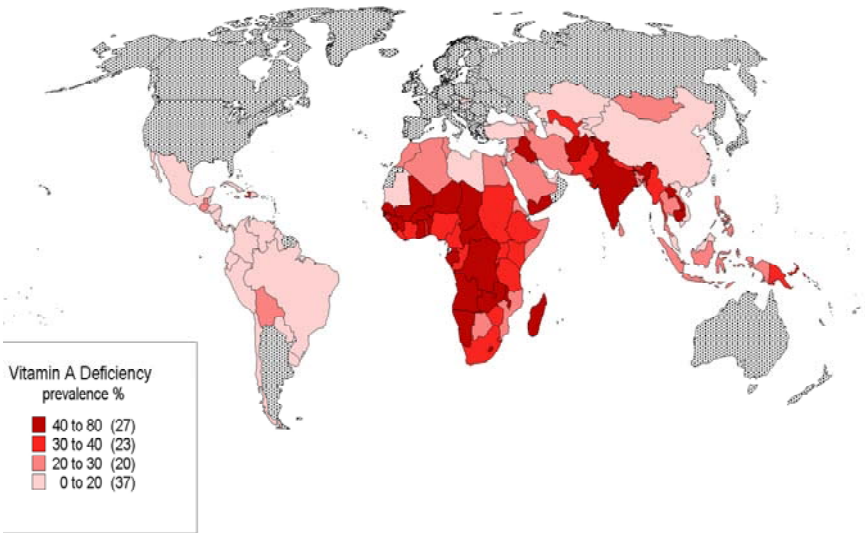


Figure 5.2: Xerophthalmia and vitamin A deficiency prevalence in children (0-72 months) respectively, in 2000 (Helwig, Rivers, Mason 2004).

Only about twenty countries that had national policies for addressing VAD also had legislation for fortification with vitamin A. Sugar and margarine, and increasingly cooking oils and flour, are the foods most often fortified. Philippines had over thirty commercial foods fortified to the extent that the packaging were entitled to carry a government label saying so, although it is unclear if the at-risk rural poor were being reached. The success of sugar fortification programmes in Central America has provided the impetus for sugar fortification to be explored as an effective intervention strategy in other developing countries (OMNI 1998, Dary & Mora 2002). Fortification of sugar with vitamin A was initiated in 1998 in Zambia and is ongoing despite economic constraints, including the falling international price of sugar and the continuous infiltration of cheaper, unfortified sugar from bordering countries. Currently, other African and Asian countries are also exploring the feasibility of sugar fortification with vitamin A (MI/UNICEF/ISO/USAID/ Swaziland Sugar Assoc. 1999). Twenty-nine developing

countries were actively fortifying, or were in advanced development stage, a range of foods with vitamin A (Mason et al. 2001) at the end of the decade.

The success of dietary diversification efforts such as home-gardening continued to be under-estimated (in the opinion of the author), although attempted evaluations of its effectiveness vary (Talukder 2000, Ruel & Levin 2000). A national survey of vitamin A in Bangladesh (a repeat of that in the early 1990s) showed that, of children not receiving a vitamin A supplement, those with a home garden, were half as likely to have symptoms of night-blindness (Bloem, personal communication 2000). Consequent to this suggested under-estimation, especially to ultimate sustainability, there have been no trend data established of such activities and they have proceeded mainly through the efforts of NGOs such as Helen Keller International (HKI 2003, 2004).

UNICEF estimated that there was a 40% decline in prevalence in vitamin A deficiency over the decade (Alnwick 1998). Vitamin A supplement coverage had increased, on average in underdeveloped countries, from around 30% only 4 years earlier (1994) to over 55%. The rate of decline of vitamin A deficiency was 'about 70% of the global rate required to eliminate clinical vitamin A deficiency by the year 2000' (Mason et al. 2001). The University of Tulane figures were 35.2% in 1995 and 33.9% or 219 million preschool children in 2000 (Mason et al. 2004). If those rates had been maintained, clinical VAD was estimated to be eliminated in South Asia by 2007, and globally by around 2015 (Mason et al. 2004). However, it was recognized that much higher rates than 70% decline would have been needed in some areas if even this were to happen. The subclinical goals would, on the other hand, need at least a couple of decades to be reached.

5.3.2 Iodine deficiency disorders

The reduction in iodine deficiency was already promising to be a global public health success story which had begun to show significant results as early as 1992 (UNICEF 1998, WHO 2004), although individual countries had started salt iodization programmes as early as the 1920s in Switzerland and the USA. Hopes were therefore high at the end of the decade, although subsequently not reached in terms of actual elimination. In the early 1990s approximately 1.6 billion or one third of the world's population were at risk of IDD (UNICEF 2001). A WHO/UNICEF/ICCIDD report (1999) identified 190

countries with a problem (41 countries had insufficient data) and 13% of the global population (c.f. the earlier 12%) or 740 million affected by iodine insufficiency as measured by TGR (total goitre rate/prevalence). That report also gave an estimate of those at risk because of the iodine status of the country as 2,225 million with IDD, especially impacting newborns born in these regions (WHO/UNICEF/ICCIDD 1999).

While the universal iodization of salt (USI), which mandates the fortification of salt for human, industrial and agricultural use, was, and is, the overwhelmingly predominant global approach. Countries have used a variety of programmes to complement this main thrust. These have included: (i) food-based approaches such as social marketing and nutrition education about iodized salt; (ii) fortification, especially the iodization of salt but also of condiments and water pots and other sources of water supply; and, (iii) supplementation with oral and intramuscular iodized oil. Other approaches have included iodization of animal fodder as in Finland (Pietinen, personal communication 2003) and salt licks, but all of these have had marginal, localized impact, and sustainability has generally been disappointing.

Figure 5.3 shows the relative size of the problem at 2000 by UNICEF Regions. The highest prevalence and numbers were again in South Asia, Sub-Saharan Africa next (SSA) and East Asia and Pacific region (EAP) showing a lower prevalence but still with large population numbers affected (Mason et al. 2004, Helwig, Rivers, Mason 2004). Prevalence in the previous USSR countries (CEE/CIS) had risen after the collapse of Communism (Gerasimov 1998) and there was a moderate problem in the Middle East and North Africa (MENA) and the Latin American and Caribbean regions (LAC). Figure 5.4 shows the geographic distribution by TGR.

Salt iodization programmes which began for many countries during the middle and second half of the last (20th) century, and other sources of dietary iodine, largely abolished this problem as a public health issue, in affluent countries that routinely iodized their salt. This experience has now been extensively adapted to many different local environments- from relatively easy adaptations by major industrial salt producers to providing support for small producers to enable them to iodize salt without losing income (Hetzel & Pandav 1997, UNICEF 1998). UNICEF estimated that among countries in the

world with a recognized IDD problem at that time (1999), all but seven had passed appropriate legislation to ensure universal iodization (UNICEF 1998).

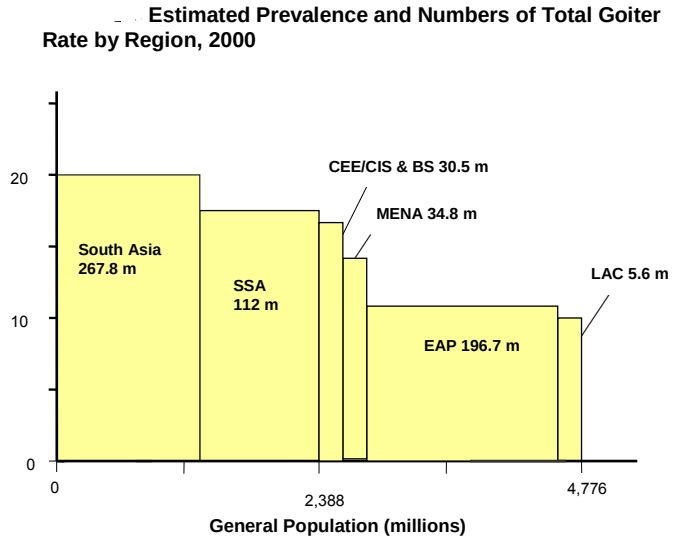


Figure 5.3 Estimated prevalence and numbers of population with iodine deficiency as indicated by presence of goitre (Helwig, Rivers, Mason 2004).

At the end of the decade, approximately 66% of all salt was being fortified, meaning that 1.5 billion people were now consuming iodized salt for the first time (UNICEF 2004, Mason, Helwig, Darnton-Hill 2004). In 1990, less than 20% of households had been using iodized salt, whereas by 2000, some 70% of households in the developing world were using iodized salt (UNICEF 2001). Although many countries continued to have significant iodine deficiency, iodized salt household coverage had gone from 10% to over 50% in Southeast Asia and to over 70% in China, with Africa being a relative success, and Europe, perhaps surprisingly, having some of the worse figures (Andersson et al. in press). Over 91 million infants each year were estimated to be protected from mental retardation, but 41 million were seen as still being unprotected. The amount of intellectual potential saved must have run into the millions of IQ points (van der Haar 1997). The number of cretins being born was estimated to have halved in the last decade, from approximately 120,000 to 60,000 annually (UNICEF 1998). Because so much of the attention was addressed to universal salt iodization (in fact, this

was mandated by UNICEF to the exclusion of other possible interventions), there are virtually no trend data on supplementation or other methods of fortification e.g. water, although supplementation is recommended for pregnant women in some countries, such as Spain, USA, and at least three countries in Asia; China, Malaysia and Thailand. Iodine status should be routinely tested for in early pregnancy where health resources permit.

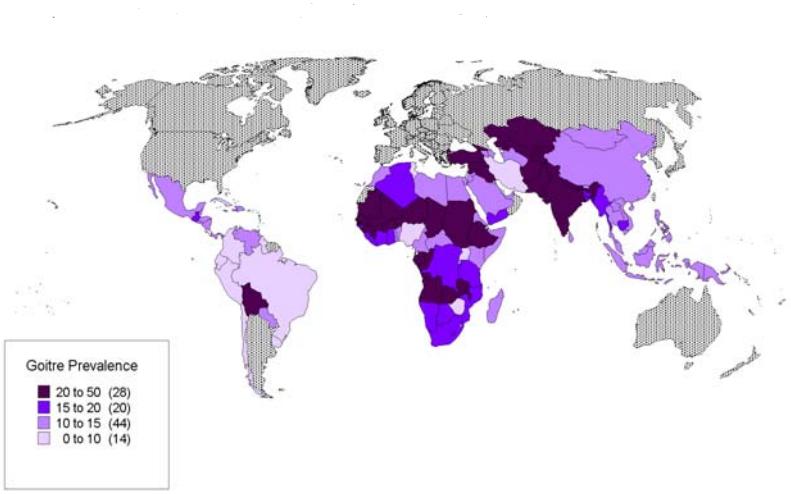
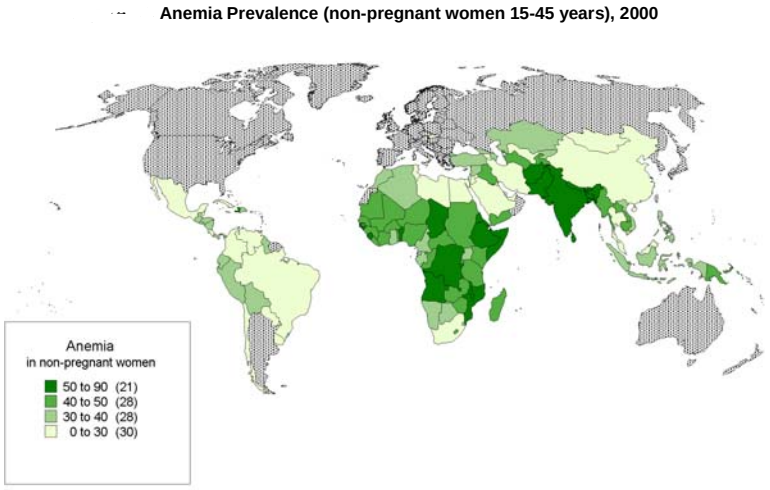


Figure 5.4: Distribution of IDD as assessed by Total Goitre Rate (general population) in 2000 (Mason et al. 2000).

5.3.3 Iron deficiency anaemia

As noted, there was no official mid-decade goal for iron or iron deficiency anaemia, probably reflecting the largely unacknowledged fact that no progress was being made. This lack of effective, large scale programmes continued to undermine attempts to prevent and control deficiencies of this micronutrient, and presumably led to the proposal not to include it in the World Fit for Children (WFFC) micronutrient goal in 2002. The final wording actually expanded a role in the prevention of anaemia but the aim of reduction by a third appears to have been as arbitrary the second time round as in the first instance.

Iron deficiency anaemia (IDA) and other anaemias were (and are) still the most prevalent nutritional problem in the world and the geographic distribution at that time is seen in the maps in Figure 5.5. Although UNICEF supplied 2.7 billion iron/folate supplements to 122 countries from 1993 to 1996, since many pregnant women enter pregnancy already anaemic, and a majority of women in the Developing World are anaemic at some stage of their pregnancy, this number of supplements was recognized as woefully inadequate, even allowing for in-country supplies. Iron deficiency anaemia was seen as probably the major public health nutrition challenge (UNICEF 1998), at least in terms of numbers which WHO estimated in 1995 to be 37% of the global population or 2,030 million people (WHO 2001). The greatest prevalences were in the South Asia, Africa and the eastern Mediterranean as are reflected in the bar charts in Figure 5.6 and the maps below (Figure 5.5).



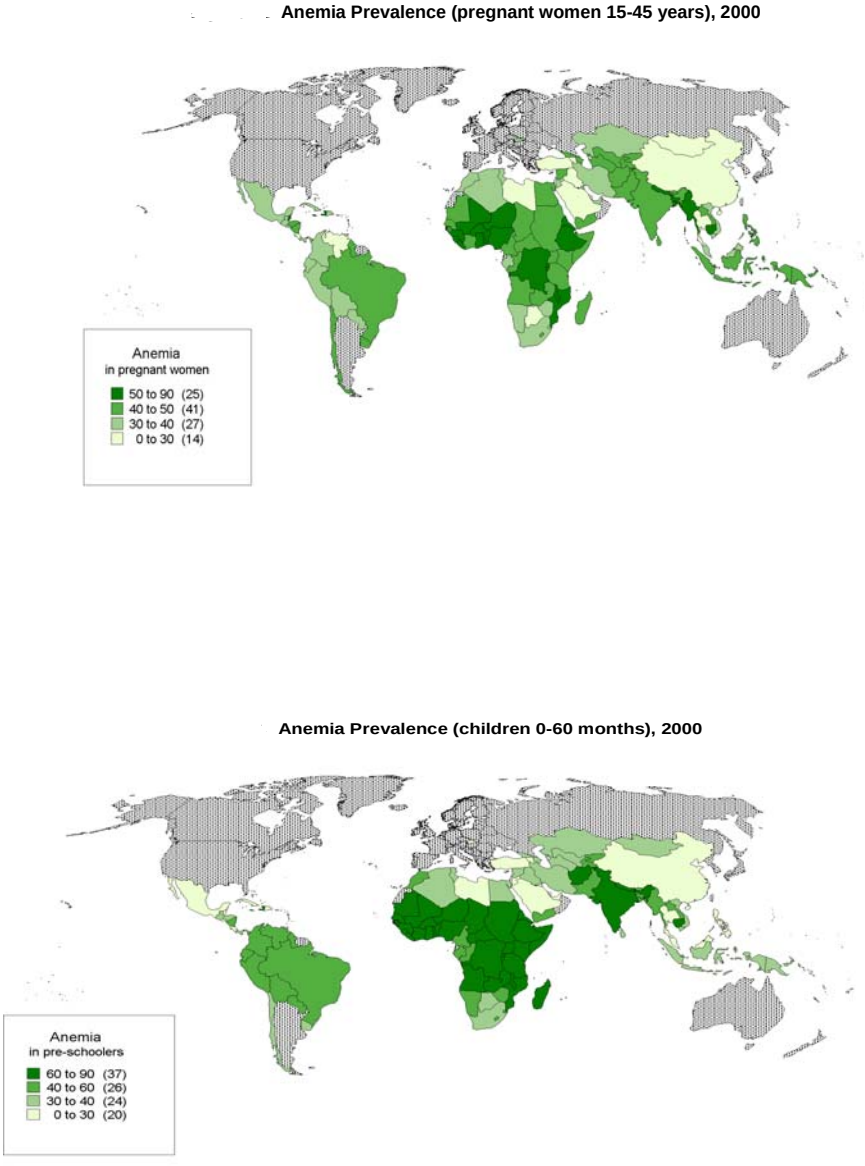
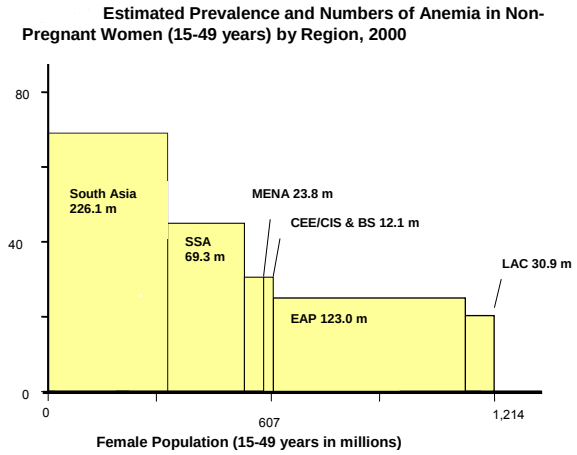
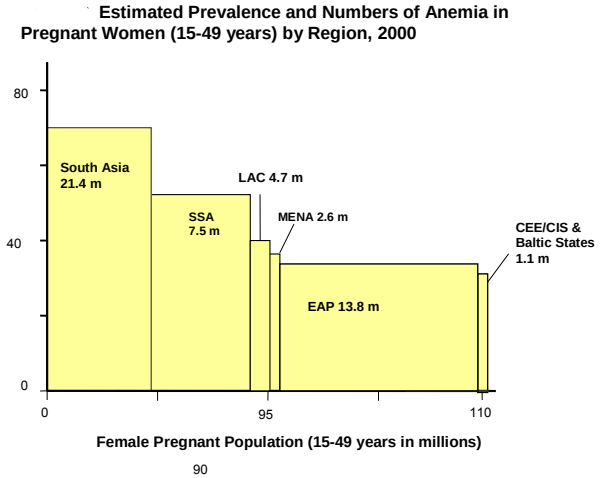


Figure 5.5: Global distribution of anaemia prevalence in non-pregnant women (15-45 years), pregnant women (15-45 years) and children (0-60 months) respectively in 2000 (Helwig, Rivers, Mason 2004)

Iron remained the micronutrient that most needed accelerated action throughout the decade, and the micronutrient goal of the World Summit for Children and the International Conference on Nutrition for reducing iron deficiency anaemia was not reached. Programmes toward the reduction of iron deficiency anaemia (IDA) included:

(i) food-based, mainly dietary diversification; (ii) fortification, especially of flour, many commercial foods, usually combined with other B vitamins and sometimes vitamin A; and currently most importantly, (iii) supplementation, in a variety of settings such as clinic-based to pregnant and lactating women, clinic-based to infants and children, private sector, factory workers, and school- aged adolescents. However coverage remained stubbornly low and so there was growing interest in issues such as compliance and supplies (Galloway & McGuire 1994, Galloway et al. 2002) and innovative attempts to increase coverage, such as intermittent versus daily dosing (Schultink et al. 1995).





90

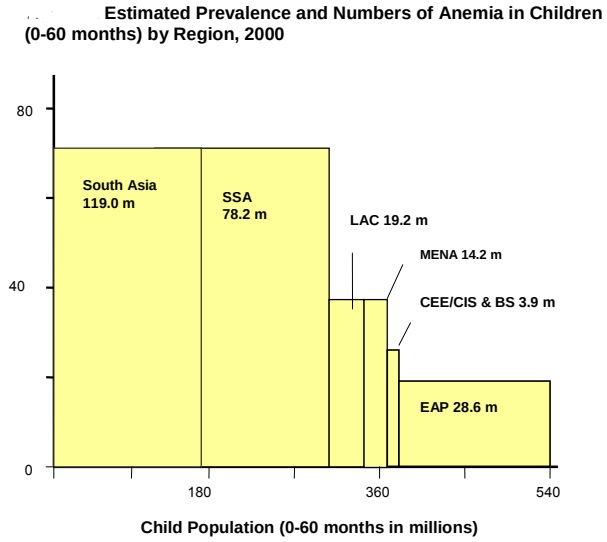


Figure 5.6: Prevalence and relative number of anaemic non-pregnant women, pregnant women and pre-school children respectively according to UNICEF Region (Helwig, Rivers, Mason 2004).

Figure 5.6 shows the prevalence of anaemia globally and by UNICEF region at that time, with high prevalences in South Asia and Sub-Saharan Africa (SSA) but with greater numbers in South Asia and East Asia and the Pacific providing the bulk of anaemic women and children.

During the decade much work was being directed towards trying to enhance delivery of iron/folic acid supplements through innovative approaches, including the private sector, as in Indonesia (OMNI 1998). USAID funding in particular favoured a social marketing approach, although this has turned out to not be generally sustainable without the considerable investment required. This has been relatively rarely picked up by the private sector, with some exceptions in Asia. Compliance issues and different regimens were also starting to move beyond research into operational research and programmes. In Malaysia, weekly supplementation over several months resolved the anaemia in over 80% of adolescent girls in a community where anaemia was highly prevalent (Tee et al. 1995), and similar results have been reported from other countries such as Indonesia (Gross et al. 1997) and Vietnam (Thu et al. 1999). Fortification of foods with iron increased and was presumed likely to have the same effect on anaemia levels, as in the

more industrialized countries' experience (Bishai & Nalubola 2002) particularly as private sector food companies started to fortify commercially. At the same time, it was being increasingly recognized that other factors must be addressed at the same time, e.g. malaria through impregnated bednets and deworming, although little to no progress was being made against malaria at that time.

Fortification with multiple micronutrients was, and is, increasingly being used as micronutrient deficiencies tend to manifest concurrently in at-risk populations. Although Latin American has been fortifying its flour with iron for some decades (Darnton-Hill et al. 1999) it has faced several challenges – technological as well as programmatic in achieving a balance between the bioavailability of the iron fortificant, its cost, and its stability in foods and probably resulted in a relatively ineffective form of iron fortificant being used. Countries of the Americas, north and south, nevertheless have extensive experience fortifying flour with iron, thiamin, riboflavin, and niacin, and more recently with folic acid and vitamin A (Darnton-Hill et al. 1999, Bishai & Nalubola 2002, WHO/FAO 2006) and wheat flour fortification was policy in most countries in Central and South America by the end of the decade (Darnton-Hill et al. 1999). Cereal flour fortification with B vitamins, iron, and sometimes vitamin A is going ahead in several Middle East countries (Verster, personal communication) and was increasingly being explored in many more throughout Asia and Africa (Nutriview 2001).

A global challenge was the lack of a clear demonstration of benefit of national iron fortification programs to at-risk population groups, including children. In 1994, Sweden ceased fortifying its bread because of a lack of perceived benefit in a replete society, although this is currently being re-evaluated (and is likely to be re-initiated) (WHO/FAO 2006). In Venezuela, fortification of wheat and corn flours with iron, B-vitamins, and vitamin A was initiated in 1993 and a preliminary survey carried out among a small group (n=307) of children in 1994 showed that the prevalence of iron deficiency anemia and anemia had decreased significantly (Layrisse et al. 1996). The mean average increase in iron intake of 6mg/day that was observed was similar to that found in other interventions in Latin America, South Africa and Thailand at that time (Beard & Stoltzfus 2001). The multi-factorial causative factors of anaemia, including non-dietary factors such as malaria and helminthes (Darnton-Hill, Paragas, Cavalli-Sforza 2007), further adds to the challenge of demonstrating a benefit of iron fortification of foods (Dary 2007). Nevertheless, thirty countries throughout the developing world had a range of

commodities (mainly wheat flour but also corn flour, milk, rice and weaning foods) that were being actively fortified with iron, to a greater or lesser degree, by the end of the decade (Mason et al. 2001).

5.4 Trends and prevalences: 1990-2010

Trends in micronutrient deficiencies were assessed for 'The Micronutrient Report' in 2001 (Mason et al. 2001), sponsored by the Micronutrient Initiative and UNICEF, and compiled by Tulane University. This work was continued in 2001-3 with further efforts identifying national survey data from the international agencies, using databases from UNICEF, WHO, the United Nations and many other sources, including 100 different government departments and agencies, especially UNICEF country offices, which were contacted with detailed instructions requesting information. This global survey yielded 49 responses. These activities all led to updated databases for additional analysis which was published in a special supplement of the Food and Nutrition Bulletin (Mason, Rivers, Helwig 2005), and was also used in the Vitamin and Mineral Deficiency Report (MI/UNICEF 2003). Full details of the methods and results can be found in a Supplement to the Food and Nutrition Bulletin (Mason, Rivers, Helwig 2005). The thesis author was then further involved (in his role as UNICEF Senior Adviser for Micronutrients at that time) by commissioning Mason's group to project further (to 2010) to help with planning at UNICEF and future budgeting (Helwig, Rivers, Mason 2004) and the last is extensively used in this section with added commentary and with further information from USAID, UNICEF and WHO. The reporting on the limited information on trends will be reported in two time periods: upto 2000 (although the actual published reports are dated later - in 2003 (MI/UNICEF) and 2004 (Mason et al.); and after 2000 to 2005 although trends are also shown extrapolated upto 2010. The World Fit for Children goals are set for 2010, apart from the goal for iodine deficiency disorders which was for 2005, and the MDGs for 2015.

The data used in several different publications, estimated regional and (in some cases) national trends in deficiencies of vitamin A, iodine, and of anaemia (as a measure of iron deficiency). Child underweight was included for context but is not reported here. Not surprisingly, there is a large degree of congruency between countries with high levels of underweight, low birth weight and high prevalences of vitamin and mineral deficiencies. Zinc and folate deficiency estimated levels, as well zinc, folic acid and multiple

micronutrient activities have been proceeding in parallel with those addressing the three other main micronutrients over the last 5 to 10 years but there is virtually no information on global trends. As noted, further trends for the three main micronutrients, which are expected to be largely positive, will be released at the end of the year (2007) from the results of the MICS and DHS data. USAID have also recently issued a 'Micronutrient Update' through MacroInternational (Mukuria & Kothari 2007) but which does not include projected trends but does include several repeat surveys. Web-based databases of WHO, UNICEF, and DHS were scanned for new survey results at that time. A review of the literature sought additional published surveys (often sub-national) generally not included in agency databases.

Three methods were used by Mason's group to estimate trends (Mason, Rivers, Helwig 2005). First, where available, comparable repeated national surveys were identified to determine trends within countries. This was followed by compiling national and sub-national survey results and obtaining unadjusted mean prevalence within regions. The third and most precise approach was first to derive estimates of prevalence at national level for every country, for defined years and biological groups, by fitting the available prevalence data to models with widely available associated variables (e.g. GNP, IMR, education, etc). The reference years were 1990, 1995, and 2000. Estimates for iodine were calculated for 1994 and 2000. Extrapolations were done from these data for UNICEF to 2010. Population-weighted aggregates to country group level were then made for the reference years. 'Best guess' estimates for each country were produced for the year 2000, to give a comparable list at one point in time - these were the estimates used in the MI/UNICEF publication 'Vitamin and Mineral Deficiencies' (MI/UNICEF, 2004) and in the previous section. Population estimates for children were taken from UNICEF State of the World's Children for the relevant years (UNICEF, 1992, 1997, 2002); for China and India the population estimates were from the UN Population Division 2002 (UN, 2002: website, accessed 2004: http://esa.un.org/unpp/ index. asp?panel=2). This source was also used for all-age populations for the IDD weighting and estimates of numbers affected.

The projections of prevalences to 2010 are based on the trends differences from 1990 to 2000; in other words they show what the picture would be if the decade 2000-2010 were to be similar to 1990-2000 (an unlikely assumption as it is turning out). The next section

shows actual data since 2000 from other sources and trends for 2000-2005 where these data exist. As will be seen, the projections were more conservative than the actual progress, presumably because of scaled-up micronutrient activities in the last 5 to 7 years.

5.4.1 Vitamin A deficiency

Surveys for xerophthalmia in pre-school age children were available for 11 countries with results for Bangladesh, Indonesia, Myanmar, Nepal and Philippines, revealing a general improvement while trends in India seemed to remain static. Trends in Laos PDR, Mongolia and Vietnam were unclear. The only other region for which repeated surveys were available was Sub-Saharan Africa, with data for two countries. Improvement occurred in Ethiopia and deterioration in Niger, the latter being surprising but may not have incorporated the later successful scaling-up of vitamin A dosing through the NIDs (Aguayo et al. 2005). Using the information available Table 5.1 shows trends by UNICEF Region (Mason et al. 2004).

Xerophthalmia, as night-blindness and Bitot's spots, according to the few repeated surveys available, declined, which also reflects informed programmatic consensus. Estimates by region show this to be so for Latin America and the Caribbean, the Middle East and North Africa, but a more static picture elsewhere in the 1990s. Putting together the various assessments, the trend predicted, at that time, was for near-elimination in the Latin America and the Caribbean region, in some countries in South Asia (e.g. Bangladesh, Nepal) and Southeast Asia. Others, notably India, appeared to remain disturbingly high, although good progress was made in the past (Reddy 1989) and the improved coverage of vitamin A supplementation noted by UNICEF SOWC reports suggested likely improvement. Recent data from India from sub-national but State-wide surveys gave figures that were lower than UNICEF estimates of coverage, and may reflect those more at risk not being reached in several States (and possible methodology problems in the national surveys, and the estimated nature of the UNICEF coverage figures).

Table 5.1: Estimated prevalence and trends of Xerophthalmia in children (0-72 months) by UNICEF Region (1990-2000) (Helwig, Rivers, Mason 2004)

Region	Percent Vitamin A Deficient			Numbers Vitamin A Deficient (Millions)			Trend (pp/yr)	
	1990	1995	2000	1990	1995	2000	1990-1995	1995-2000
South Asia	1.47	1.33	1.69	2.92	2.72	3.47	-0.03	0.12
Sub-Saharan Africa	1.75	1.54	1.54	2.09	1.99	2.05	-0.04	0.00
Middle East & North Africa	1.23	0.91	0.85	0.55	0.45	0.39	-0.06	-0.01
East Asia & Pacific	0.68	0.40	0.47	1.45	0.78	0.87	-0.06	0.01
Latin America & Caribbean	0.61	0.59	0.28	0.40	0.38	0.17	-0.00	-0.06
CEE/CIS & Baltic States	----	0.40	0.35	----	0.08	0.06	----	-0.01
Total	1.2	1.0	1.1	7.40	6.39	7.00	-0.04	0.02

Consistent improvement in levels of vitamin A deficiency (measured as serum retinol <0.7 µmol/L) was estimated to have occurred in all regions, with greater improvements seen during the earlier part of the decade (Table 5.2). South Asia demonstrated the greatest improvement, nearing a 7 ppt (percentage point) decline for the time period analyzed. In spite of substantial improvement, prevalence for this region remained the highest, with nearly half of the child population affected.

Table 5.2: Estimated prevalence of vitamin A deficiency in children (0-72 months) by UNICEF Region (1990-2000) (Helwig, Rivers, Mason 2004).

Region	Percent Vitamin A Deficient			Numbers Vitamin A Deficient (Millions)			Trend (pp/yr)	
	1990	1995	2000	1990	1995	2000	1990-1995	1995-2000
South Asia	56.6	52.3	49.8	112.4	106.8	102.2	-0.86	-0.50
Sub-Saharan Africa	42.3	41.4	40.8	50.6	53.5	54.3	-0.18	-0.12
Middle East & North Africa	32.6	29.0	28.0	14.5	14.3	12.9	-0.72	-0.20
East Asia & Pacific	22.7	22.2	20.0	48.3	43.3	36.9	-0.10	-0.44
Latin America & Caribbean	20.1	16.8	14.8	13.0	10.6	9.1	-0.66	-0.40
CEE/CIS & Baltic States	----	22.0	22.0	----	4.4	3.6	----	0.00
Total	37.3	35.2	33.9	238.8	232.9	219.0	-0.42	-0.26

When UNICEF first began reporting on progress through The State of the World's Children report in 2000, global coverage with at least one dose was approximately 50%, through linkages of vitamin A supplementation with National Immunization Days (NIDs) for polio eradication. Although NIDs helped guarantee delivery of one high dose supplement, only 18 countries were distributing the requisite second dose by 1999, roughly translating into 16% of children receiving supplements as per international recommendations. The projections to 2010 in figure 5.7 show a reduction overall but a possible increase in South Asia. Although concern was expressed by many (as noted in earlier chapters) that progress would falter with the phase-out of polio NIDs, coverage actually has steadily improved in recent years, as will be seen in next section (Dalmiya, Palmer, Greig 2006).

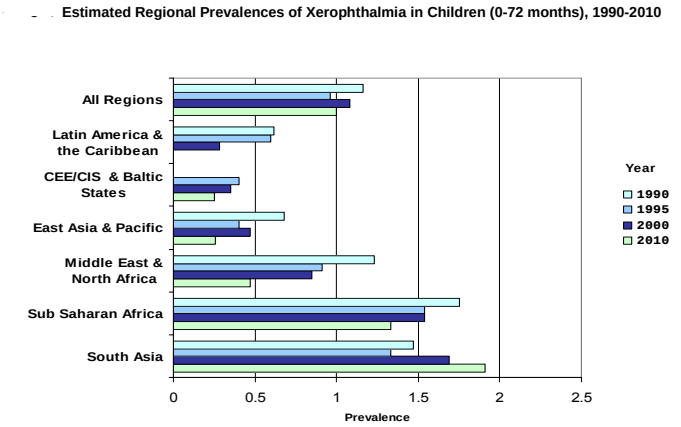


Figure 5.7: Estimated UNICEF Region al prevalences of xerophthalmia in infants and children (1990-2000) (Helwig, Rivers, Mason 2004).

5.4.2 Iodine deficiency disorders

Levels of iodine deficiency disorders measured as total goitre rate dramatically declined during the period analyzed with estimated regional prevalences of total goitre rate (TGR) for 1994 and 2000 are presented in table 5.3. Urinary iodine excretion is increasingly used to assess population iodine status, and the results compiled by WHO (WHO 2004, de Benoist et al. 2005) are shown in Table 5.7.

However, at that time, iodine nutrition prevalence was measured most often by TGR and this rate or prevalence remained high in South Asia, where the overall prevalence remained static between 1994 and 2000 at almost 20%, the highest prevalence of all regions. This represented over 267 million people in 2000. South Asia without India was estimated to have decreased in prevalence over this period, while India's salt iodization coverage is reported to have fallen from about 70% in 1994 to 50% in 2000 due to political events, associated with an estimated increase in goitre prevalence (see Figure 5.17). Being a country with a population the size of India's this affected apparent global progress in reducing IDD prevalence.

Many countries in Sub-Saharan Africa improved their iodized salt coverage over this time from an average of 43% in 1994 to 59% in 2000 and this trend has continued

(Mason et al. 2004, WHO 2004, de Benoist et al. 2005). Total goitre prevalence declined during the same time period at an average of 0.72 ppts per year, although WHO trend data did not identify this (WHO 2005) and this is discussed in the next section. The Middle East/North Africa group appeared to be more static at around 12 to 14% TGR but with a 75% average iodized salt coverage.

Table 5.3: Estimated prevalence of Total Goitre Rate in the general population and household salt iodization by UNICEF Region (1994-2000) (Helwig, Rivers, Mason 2004).

	1994 (1992-1996)		2000 (1997-2002)		
Region	**Average HH Salt Iodization**	**Average TGR**	**Average HH Salt Iodization**	**Average TGR**	**Trend (pp/yr)**
South Asia	58.5	18.7	48.8	19.8	0.18
Sub-Saharan Africa	43.1	21.6	59.4	17.3	-0.72
Middle East & North Africa	75.6	12.0	75.5	14.0	0.33
East Asia & Pacific	49.1	18.7	80.7	11.2	-1.25
Latin America & Caribbean	82.0	12.1	88.6	9.7	-0.4
CEE/CIS & Baltic States	17.1	16.2	24.0	16.6	0.07
All Regions	64.7	17.6	75.3	14.4	-0.53

There had been forty-four comparable repeat surveys for total goitre rate that showed that in 37 of the 44 countries iodine deficiency disorders were clearly improving, in many instances dramatically. In Thailand, levels of household salt iodization went from 1% in 1986 to 75% by the year 1996. This resulted in a 1.1 percentage point per year decrease of total goitre rate, going from 17% in 1986 to 2.7% for the 1999 survey. Dramatic improvement was also seen in several other countries including Benin, Bhutan, Bolivia, Honduras, Indonesia, Madagascar, Nicaragua and Vietnam (Mason et al. 2004).

Iodine deficiency disorders prevalence was clearly declining as household salt iodization programmes expanded. The relationship between salt iodization and a decrease in

goitre prevalence was clear from Mason et al.'s report (although less so from the WHO 2004 analysis report) which observed that the TGR/P fell in line with iodization (Mason et al. 2004). Evidence suggests that countries reaching 90% iodization or so generally have total goitre prevalences of less than 10%; countries with iodization coverage reaching 50 or 60% have considerably higher levels.

The apparent global trend, from 18% in 1994 to 14% in 2000 probably understated the improvement. However, the WHO Report showed a 4% increase from 1993 to 2003 (WHO 2004) but, apart from masking decreases in the WHO Regions of the Americas and the Western Pacific, the apparent anomaly can partly be explained (and is addressed again later in the next section). Firstly, there may be a reporting bias so that as more surveys were included more goitre was found. Secondly, the pre-iodization (endemic) goitre rate before 1994 which is the first estimate here, was likely to have been nearer 30% for developing regions (WHO/UNICEF/ICCIDD 1993). Since IDD prevalence probably only changes with implementation of an intervention such as iodized salt, it is likely that the actual comparison should be the current 14% prevalence rate compared with the 30% expected without salt iodization. The University of Tulane therefore concluded that salt iodization had probably halved the extent of IDDs by the end of the decade.

Projections to 2010 can be seen in Figure 5.8, together with regional prevalence estimates for 1994 and 2000. It was presumed salt iodization would continue to expand while noting this may well become more difficult as the harder-to-reach areas and population groups are those presently less covered. If they had indeed continued to expand at the same rate, then further substantial drops in IDDs would have been expected. As will be seen, there appeared to be a definite plateauing of household coverage. Nevertheless, the past decade saw dramatic progress in the campaign to eliminate iodine deficiency from the beginning of the decade, despite the unexpected WHO negative trend which may reflect, amongst other factors, the unsuitability of TGR for monitoring purposes (Zimmermann et al. 2000, Hetzel et al. 2004, ICCIDD 2006, Andersson et al. in press). In 1990, few developing countries had large-scale salt iodization programmes and, as a consequence less than one in five households were estimated to consume adequately iodized salt. As a result about 1.7 billion people (or

32% of the developing world's population) were estimated to be at risk of iodine deficiency (UNICEF 2006).

Based on data from a total of 97 countries in the developing world between 1998 and 2004, covering 95% of the developing world population, a UNICEF nutrition report concluded that while in the early 1990s only around 20% of households consumed adequately iodized salt, ten years later more than two-thirds (69%) of households in the developing world were consuming iodized salt, and 82 million newborns were therefore estimated to be protected from learning disabilities caused by the iodine deficiency disorders (based on estimates from 1998-2004) (UNICEF 2006). However, large differences exist in the consumption of adequately iodized salt among regions of the developing world. The highest levels are being identified in Latin America and the Caribbean (86%) and East Asia and the Pacific (85%), with the lowest levels in CEE/CIS (47%). In Sub-Saharan Africa almost two-thirds of households consume adequately iodized salt (64%) (UNICEF 2006).

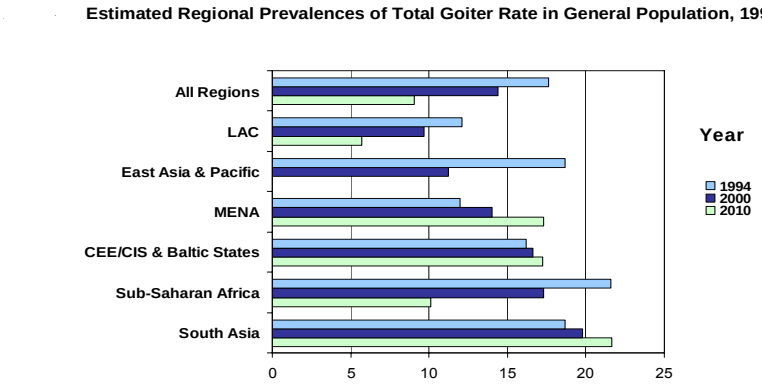


Figure 5.8: Estimated trend of total goitre rates by UNICEF Region in the general population (1990-2010) (Helwig, Rivers, Mason 2004).

Figure 5.8 shows the predicted trends of total goitre prevalence. These somewhat mirror the salt iodization coverage trends. Both South Asia, largely because of India, and the CEE/CIS UNICEF Region, largely because of the Russian Federation and Ukraine, were predicted to have increasing prevalence. This was probably too

pessimistic due to changes in legislation in India and impressive increases in the Central Asian Republics.

Combining all sources, it is seen that real progress had been made over the decade and in an increasing number of countries. The WHO Report showed (as indicated by UI levels) 72 countries with optimal iodine nutrition or more, and a further 40 with only mild iodine deficiency (WHO 2004). It is likely that this is continuing to improve given the latest UNICEF State of the World's Children data with 33 countries now with greater or equal to 90% coverage with USI and (from 123 countries with data) a total of just over half (50.4%) having at least 75% of their households consuming iodized salt (UNICEF SOWC 2007 unpublished).

5.4.3 Anaemia

Levels of anaemia in 2000 in pregnant and non-pregnant women, and children, are shown in Tables 5.4, 5.5 and 5.6 (Mason et al. 2004). While some improvement was apparent, prevalences remained very high at 40% or above for all developing regions combined in each group assessed. This represented over 485 million non-pregnant women, almost 280 million children (0 to 60 months) and 48 million pregnant women in the year 2000. Prevalences in South Asia in 2000 for pregnant and non-pregnant women were above 65% and in children of this region almost 70%. For non-pregnant women, prevalence did not appear to improve until the latter half of the decade, when an average of over 0.5 percentage point (ppt) improvement occurred each year and possibly was starting to reflect increasing prosperity for some in those societies. In pregnant women an improvement of 0.4 ppts per year occurred during the same time period. The most improvement in this region occurred in children, with an average yearly improvement of 0.74 ppts between 1995 and 2000. The data are reflected in Tables 5.4, 5.5 and 5.6. Nevertheless, projected trends showed a global increase in pregnant women (Figure 5.10) with slightly more encouraging trends in non-pregnant women (Figure 5.9) and infants and young children (Figure 5.11).

Sub-Saharan Africa, where very high prevalence was seen in children, 70.5%, demonstrated an improvement of 0.4 ppts per year for the latter part of the decade, yet

remained relatively static or showed an increase in prevalence for women and non-pregnant women.

Table 5.4: Estimated Prevalence of Iron Deficiency Anemia in Non-Pregnant Women (15-49 years) by UNICEF Region (1990-2000) (Helwig, Rivers, Mason 2004).

	Percent Iron Deficient			Numbers Iron Deficient (Millions)			Trend (pp/yr)	
Region	1990	1995	2000	1990	1995	2000	1990-1995	1995-2000
South Asia	69.5	70.7	68.2	182.6	208.5	226.1	0.26	-0.52
Sub-Saharan Africa	43.6	45.6	46.5	49.1	59.3	69.3	0.4	0.18
East Asia & Pacific	30.0	26.9	25.1	127.0	123.7	123.0	-0.61	-0.36
Middle East & North Africa	28.8	31.2	31.5	16.0	20.1	23.8	0.48	0.06
Latin America & Caribbean	26.1	23.2	24.0	30.0	27.0	30.9	-0.59	0.16
CEE/CIS & Baltic States	--	26.5	31.1	--	9.3	12.1	--	0.9
Total	41.7	40.7	40.0	404.7	447.9	485.2	-0.20	-0.16

Table 5.5: Estimated Prevalence of Iron Deficiency Anemia in Pregnant Women (15-49 years) by UNICEF Region (1990-2000) (Helwig, Rivers, Mason 2004).

Region	Percent Iron Deficient			Numbers Iron Deficient (Millions)			Trend (pp/yr)	
	1990	1995	2000	1990	1995	2000	1990-1995	1995-2000
South Asia	67.5	67.3	65.9	18.8	20.3	21.4	-0.04	-0.40
Sub-Saharan Africa	47.9	48.2	48.2	6.3	6.9	7.5	0.06	0.00
Middle East & North Africa	35.1	39.4	35.1	2.1	2.6	2.6	0.86	-0.86
East Asia & Pacific	34.9	31.7	31.9	13.6	13.0	13.8	-0.64	0.04
Latin America & Caribbean	36.6	39.0	41.0	3.6	4.1	4.7	0.48	-0.40
CEE/CIS & Baltic States	----	32.2	30.5	----	1.1	1.1	----	-0.34
Total	43.7	45.3	45.1	41.8	48.0	51.1	-0.22	-0.04

Of the nine countries with repeated national surveys in children (0-59 months), six demonstrated improvements (Bangladesh, Jamaica, Kazakhstan, Peru, Thailand and Viet Nam), two showed possible deterioration, (Panama and Philippines) and no real change was determined in Honduras. A larger number of surveys were available for anaemia in non-pregnant and pregnant women. For countries in the South East Asia and Pacific region including Indonesia, Philippines, Thailand and Viet Nam, a general improvement was seen in non-pregnant women, but an apparent deterioration in pregnant women. Results for pregnant women in Thailand are available for eight national surveys. Of these, the four surveys conducted in the decade of the nineties suggest an improvement rate of over 1 percentage point per year between 1991 through 1996.

Table 5.6: Estimated prevalence of iron deficiency anemia in children (0-60 months) by UNICEF Region (1990-2000) (Helwig, Rivers, Mason 2004).

Region	Percent Iron Deficient			Numbers Iron Deficient (Millions)			Trend (pp/yr)	
	1990	1995	2000	1990	1995	2000	1990-1995	1995-2000
South Asia	74.6	73.3	69.6	123.5	124.8	119.0	-0.23	-0.74
Sub-Saharan Africa	72.1	72.5	70.5	71.8	78.1	78.2	0.08	-0.4
Middle East & North Africa	40.3	41.2	37.2	15.1	16.9	14.2	0.18	-0.8
East Asia & Pacific	27.6	21.0	18.6	48.9	34.2	28.6	-1.32	-0.48
Latin America & Caribbean	43.4	39.4	37.4	23.4	20.8	19.2	-0.8	-0.33
CEE/CIS & Baltic States	--	27.8	28.2	--	4.6	3.9	--	0.08
Total	53.0	50.7	48.8	282.7	279.4	263.1	-0.46	-0.38

In non-pregnant women in Indonesia, Thailand, and the Philippines, the prevalence rose between the late 1970s and 1980s and then fell again between the 1980s and the 1990s, showing improvements in the latest surveys. Viet Nam has shown striking improvement since 1995, with the prevalence apparently dropping from 41% to 24% in 5 years (an improvement of 3.4 ppts per year). Other countries showing improvement are Bangladesh (a 36 percentage point reduction in prevalence over 20 years), India, which appears to have been improving since the mid-1980s, and Kazakhstan, which saw a drop in prevalence of about 13 ppts over four years (about the same rate of improvement as Viet Nam). Countries showing worsening trends included Colombia, The Gambia, Kenya, and Venezuela.

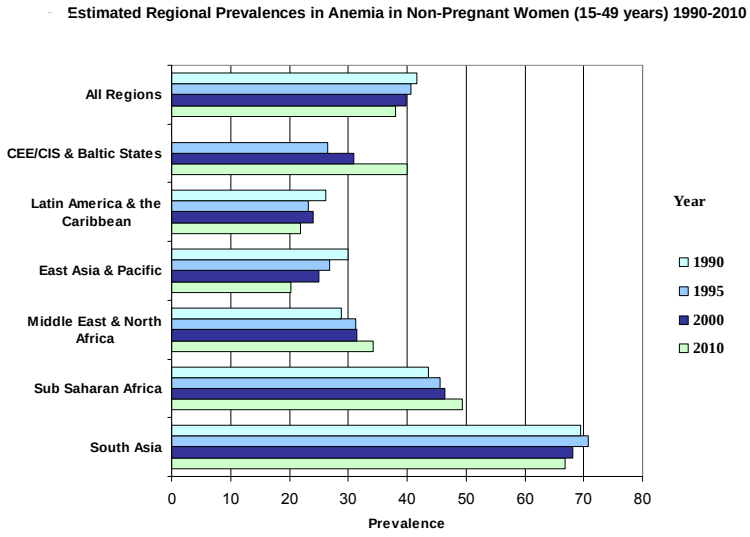


Figure 5.9: Predicted trends in anaemia prevalence in non-pregnant women (15-49y) by UNICEF Region (1990-2010) (Helwig, Rivers, Mason 2004).

The report noted that pregnant women are more often monitored than other groups in the population for haemoglobin status and therefore more data and repeated surveys are generally available for this group. Some countries showed recent improving trends Guyana, for example, has consistently shown improvement since the late 1970's, but the prevalence was still very high (more than 50% in 1997 survey), whereas Viet Nam showed dramatic improvement, with a drop in prevalence of 20 ppts over 5 years. Stable prevalence levels were seen in pregnant women in Costa Rica, Indonesia, Jamaica, Myanmar, and elsewhere. Prevalence among pregnant women in The Gambia increased from 60% in 1987 to 73% in 2001. Levels of anaemia in children in Sub-Saharan Africa and South Asia remained strikingly high, and in Sub-Saharan Africa

were extremely high for children, around 70%.

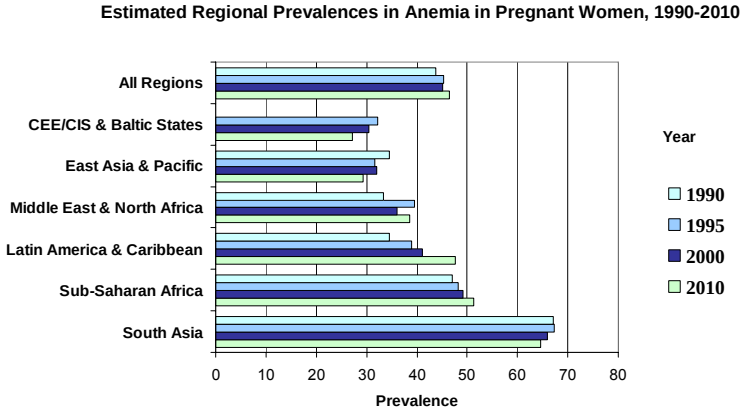


Figure 5.10: Estimated trends for anaemia in pregnant women (15-49y) by UNICEF Region (1990-2010) (Helwig, Rivers, Mason 2004).

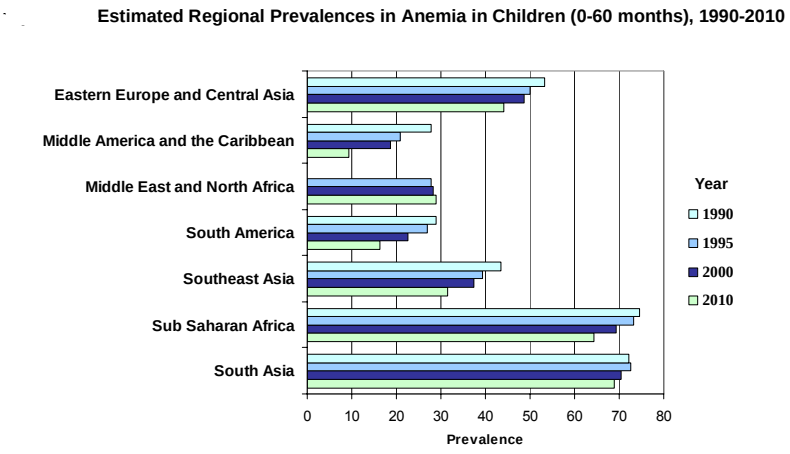


Figure 5.11: Estimated trends for anaemia in infants and young children (9-60m) by UNICEF Region (1990-2010) (Helwig, Rivers, Mason 2004).

The projections of anemia prevalences to 2010, done by Mason et al. (2004) for UNICEF were that prevalences would remain high, and even increase, if the decade of 2000 to 2010 continued to be like the 1990's. Children and women would continue to be seriously affected, and anaemia in pregnant women was thought likely to even increase, with one third to one half affected. Even in Latin America and Caribbean, otherwise showing improvement in micronutrient deficiencies, anaemia was increasing in pregnant women. Nevertheless, there were some encouraging success countries such as Bangladesh, Thailand and Vietnam. Trends for Africa were predicted to show little change or even worsen.

5.5 Progress towards the UN Special Session for Children Micronutrient Goals leading into the new Millennium (2000-2010)

The predicted trends showed improvements in vitamin A deficiency prevalence although little shift in xerophthalmia, improvement in total goitre prevalence, and very slight improvement in anaemia levels. However current available data show a somewhat more optimistic picture in many cases halfway through this decade, reflecting the substantial effort and resources put in by countries, agencies and donors. A great deal of new data will be released later this year (2007) largely to report to the UN Special Session on progress towards the earlier goals (the World Fit for Children Goals). In the meantime, information available since the earlier efforts, which were largely based on data up to 2000 and extrapolations from any trend data, will be briefly explored, along with a reminder of the appropriate goals from the UN World Fit for Children (WFFC) goals of 2002 (UNICEF 2001). Data and trends are presented, up to 2005 where available, especially for vitamin A and iodine including some preliminary information for the State of the World's Children 2007 report, with little data on progress on iron, zinc, folate and the implementation of multiple micronutrient interventions.

5.5.1 Vitamin A deficiency

"Achieve sustainable elimination of …vitamin A deficiency by 2010'

Vitamin A supplementation is high among the key interventions of the Lancet Child Survival Series, achievable at a large-scale, and with proven potential to reduce the number of preventable child deaths each year (Jones et al. 2003) and so has recently

received wider attention (Dalmiya, Palmer, Darnton-Hill 2006). It has also been described as one of the most cost-effective interventions for improving child survival (Edejer et al. 2005). A recent internal report from UNICEF provided an update on global efforts to ensure full protection (defined as preventive vitamin A supplements twice annually) to all children 6-59 months in over 100 priority countries (Dalmiya, Palmer, Greig 2006). Progress is being tracked using the agreed-upon UNICEF and WHO indicator for vitamin A supplementation coverage: the proportion (%) of children 6-59 months receiving at least one high-dose vitamin A supplement in the past six months. Coverage data were drawn from figures reported in the UNICEF Annual Reports of the State of the World's Children (SOWC) for 1999 through 2004, along with global and regional trends for the same period. Progress in vitamin A programming was also considered for the subset of 60 countries that UNICEF has designated "high priorities" for the scale-up of child survival efforts but which are not reported here in any detail (but will be available when the report is published as a UNICEF document this coming year). DHS also released a "Micronutrient Update" in January 2007 which updated some countries' data of vitamin A supplementation (Mukuria & Kothari 2007). WHO is in the progress of updating its global database on vitamin A (WHO VMNIS 2007).

The UNICEF report on progress in vitamin A programmes (Dalmiya, Palmer, Greig 2006), focussed on vitamin A supplementation in 103 priority countries which met at least one of the following criteria: where the U5MR exceeds 70 deaths per 1,000 live births (61 countries); 35 additional priority countries selected due to an elevated prevalence of VAD (vitamin A deficiency), based on data from national-level assessments registered in WHO's Vitamin and Mineral Nutrition Information system (WHO 2004); and, seven countries (the Democratic People's Republic of Korea, Indonesia, Kyrgyzstan, the Occupied Palestinian Territory, Thailand, Uzbekistan and Vietnam) where, although not meeting the criteria above, the governments have recognized VAD as a public health problem and are committed to vitamin A programming. Significant reductions in under-five mortality and VAD have been achieved in some of these countries, partly as a result of ongoing supplementation efforts (West 2002, Ahmed & Darnton-Hill 2004, West & Darnton-Hill 2007).

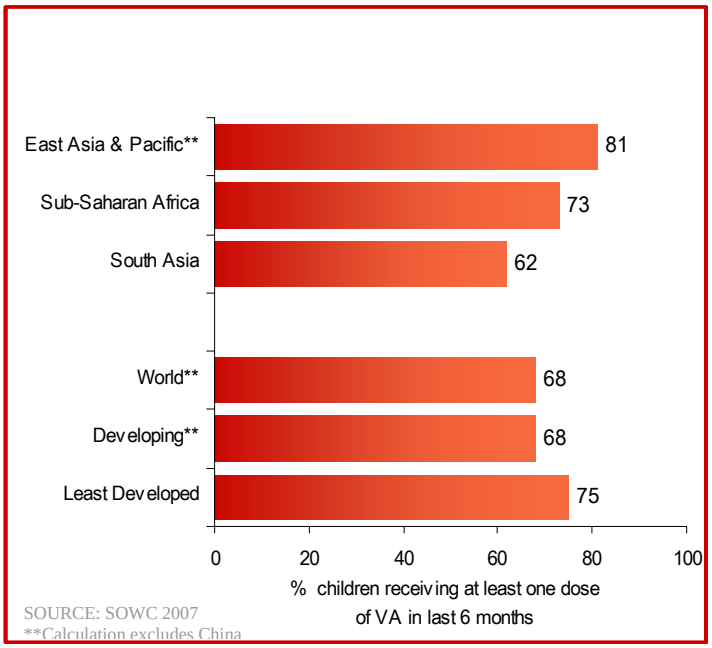


Figure 5.12: Percentage of eligible children (6-59m) receiving at least one dose of vitamin A in the previous six months in 2004 (Dalmiya, Palmer, Greig 2006)

In 2004, approximately 190 million children received at least one high-dose vitamin A supplement, representing a global coverage of 68% of eligible children. Supplementation programmes to children living in the least developed countries of the world reached approximately 75% of targeted children with at least one capsule in the last six months (Figure 5.12), but even as affected areas of the world approach adequate levels of one-dose coverage, millions of children are still not fully protected with the recommended two annual doses. The report estimated that only 26 of the 103 priority countries attained protective coverage levels in 2004, defined as reaching at least 70% of children with two rounds of supplementation. More specific information on regional coverage can be found in the report of Dalmiya, Palmer and Greig for UNICEF (2006).

Supplementing these results are those repeat studies from DHS (Mukuria & Kothari 2007). Their figure for overall average was 76.5% of all eligible children (6-59 months) getting vitamin A within the 6 months preceding the survey. The range in Sub-Saharan Africa was from 33.3% in Cameroon to 78.4% in Ghana. The coverage figures were, perhaps unexpectedly, similar for 6-11 month infants, if slightly lower. Where there have been repeat surveys the increases are striking. From 0.7% in Chad in 1996/97 to

34.3% in 2004; from 2.3% to 76.2% in Madagascar and from 0.5% to 40.8% in Mali in 2001. In other regions, coverage levels were not much changed except in Indonesia where coverage went from 41.6% in 1997 to 75.1% in 2002/03. Egypt showed little change from a low 12.6% to 11.1% five years later; Bangladesh from 79.3% to 78.5% and Philippines 75.6% to 76.0% (Mukuria & Kothari 2007).

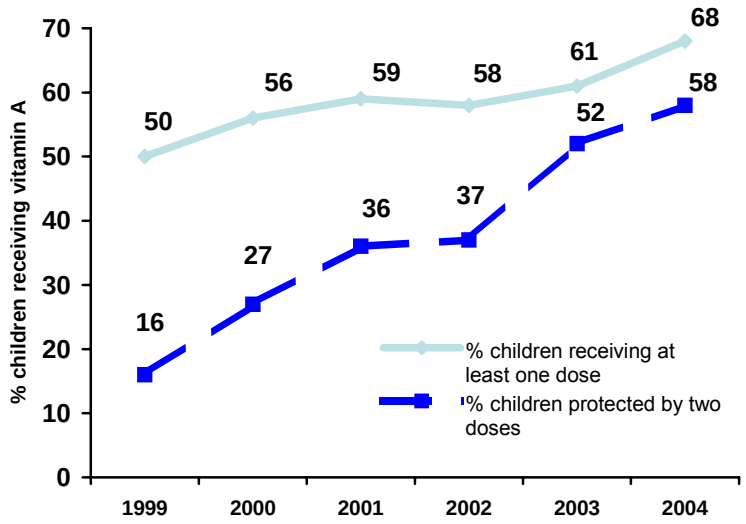


Figure 5.13: Percentage of eligible children 6-59 months receiving two doses of vitamin A (Dalmiya, Palmer, Greig 2006 based on UNICEF data)

When UNICEF first began monitoring global coverage in 1999, only 16% of children were fully protected with two annual doses of vitamin A. Coverage has increased dramatically over the past decade, with approximately 58% of children now receiving the recommended two annual doses (Figure 5.13). Gains can be attributed to innovations in vitamin A delivery, such as integrated child health packages, which have been particularly successful and started in the least developed countries of the world (Aguayo et al. 2005). Progress has also been achieved in building sustainable programmes: one-third of countries are contributing to the operational costs of supplementation, a growing number are procuring capsules from national budgets, and capsule supply management is increasingly efficient. In an important development, substantial advocacy efforts, particularly in eastern and southern Africa countries, have led to the inclusion of vitamin A supplementation in poverty reduction strategies and coordinated health sector investment approaches (Dalmiya, Palmer, Darnton-Hill 2006).

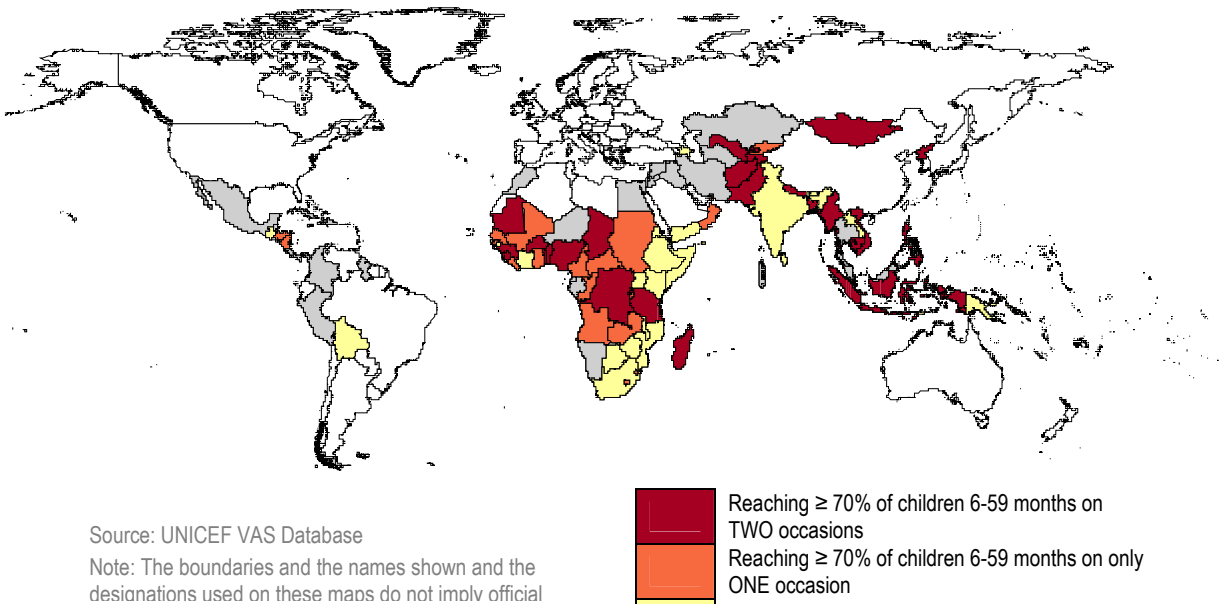


Figure 5.14: Vitamin A supplementation country-level coverage as at 2004 (Dalmiya, Palmer, Greig 2006)

While this report illustrates important gains over the past decade, much in the last three years, there are still millions of children not receiving the recommended two annual doses. These children are presumed to be at risk of vitamin A deficiency, as few countries have been able to establish the dedicated delivery strategies for vitamin A necessary for sustained effective coverage. Evidence from UNICEF's MICS also suggests that children living in poor, rural areas – those likely to be at greatest risk – may be disproportionately missed by the intervention. Supplementation of women in the post-partum period lags far behind programmes for young children, even though opportunities such as newborn immunization contacts clearly exist to reach this target group, protecting both mothers and their newborns from inadequate vitamin A stores. The unpublished figures for 2007 show a very encouraging increase to 72% of all eligible children with two doses of vitamin A (and 77% in the least developed countries) (UNICEF SOWC 2007). The map in Figure 5.14 shows coverage at the end of 2004 (Dalmiya, Palmer, Greig 2006) based on earlier State of the World's Children data from the 2006 report.

Nevertheless, further analysis of these encouraging figures suggest some on-going challenges. The summary coverage estimates often mask problems in reaching the most disadvantaged children and those most in need. While the internal UNICEF report

noted that MICS cannot always provide accurate coverage figures for vitamin A supplementation – surveys are rarely carried out immediately following a distribution, limiting a mother's ability to recall whether or not her child was reached – they are useful to explore any systematic differences in which children were supplemented (Dalmiya, Palmer, Greig 2006). Based on a review of vitamin A supplementation coverage data gathered through MICS in 26 of the 103 VAS target countries, there was no evidence of differential coverage between boys and girls. However, slight differences in coverage were apparent between children living in urban and rural areas, with rural children approximately 10% more likely to have never received a vitamin A supplement than their urban counterparts. Similarly, children from poorer families were more likely to have never received vitamin A as compared to children from relatively better-off families.

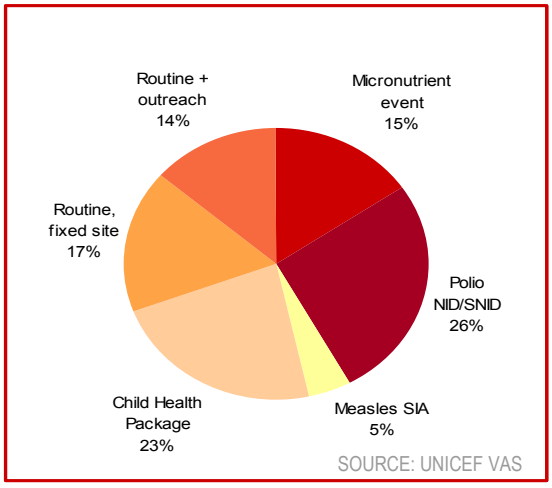


Figure 5.15 Proportion of total vitamin A delivery attempts in 2004, by strategy (Dalmiya, Palmer, Greig 2006)

All but two of the 26 MICS countries were delivering vitamin A through campaign-style events at the time of the MICS data collection. Campaigns are likely to produce increased equalization of health care, reaching the majority of children across all subgroups. However, the evidence suggests some disparities even with campaign-style approaches in failing to reach some of the rural poor, and so continuing attention is being paid to supplementation delivery strategies and equity.

One of the greatest challenges for vitamin A has been the search for sustainable mechanisms to deliver supplements. As noted in earlier chapters, vitamin A supplementation was first linked with the Poliomyelitis National Immunization Days (NIDs) in the late 1990s. Despite concerns about the phasing out of these campaigns, NIDs remained the most prominent strategy in 2004, accounting for 26% of all delivery attempts. However, as polio eradication is gradually achieved and integration of vitamin A supplementation with NIDs becomes less of an option in some areas, countries are seizing on a more diverse set of delivery opportunities (Figure 5.16).

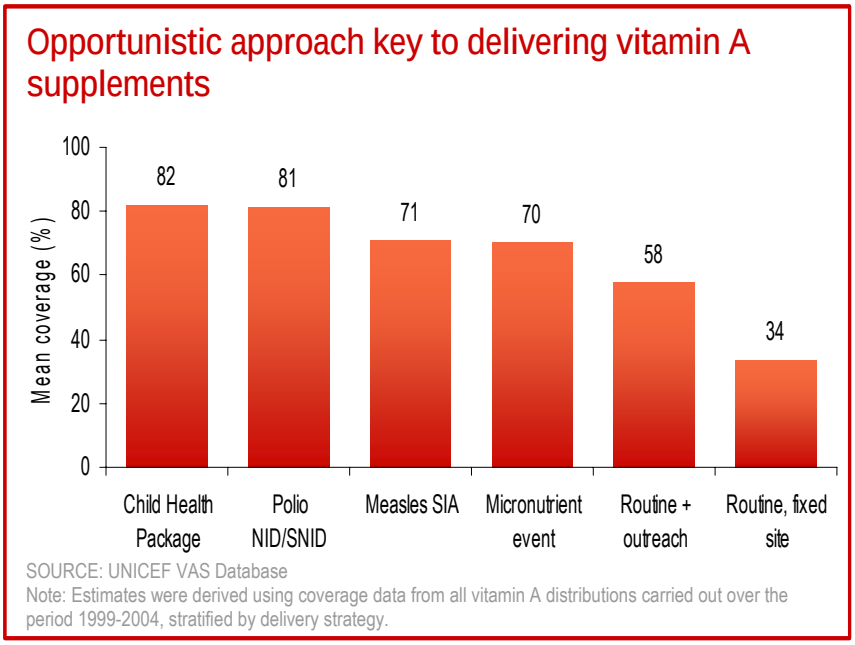


Figure 5.16: Mean one-dose coverage using different delivery mechanisms (1999-2004) (Dalmiya, Palmer, Greig 2006).

Efforts are continuing to integrate vitamin A supplementation into routine health services. While immunization programmes have been a strong partner in reaching children under the age of one, EPI (the Expanded Programme on Immunization) alone has proven to be insufficient to reach all targeted children from six to 59 months of age, twice annually (Dalmiya, Palmer, Darnton-Hill 2006). This is clearly reflected in mean coverage rates among countries relying solely on routine delivery (Figure 5.16) where routine fixed site services reach only a third of eligible children. Until routine health services can reach over 70% of all targeted children on a regular basis, outreach and pulse events will continue to be critical to deliver vitamin A (Dalmiya, Palmer, Greig 2006). Delivery of vitamin A with other child survival interventions – de-worming, bed-net distribution, or

outreach efforts initiated by other programmes – has continuously achieved the highest coverage rates and may serve as a model for the integrated delivery of high impact interventions (Dalmiya 2007).

Post-partum vitamin A supplementation lags behind the efforts to reach young children with vitamin A. Programmes exist in only two-thirds of priority countries and most are limited in scope. In 2004, only twelve priority countries surpassed 50% coverage: Azerbaijan, Benin, Cape Verde, Egypt, Honduras, Marshall Islands, Morocco, Myanmar, Oman, Sao Tome and Principe, Tajikistan and Viet Nam (Dalmiya, Palmer, Greig 2006). Of the 26 countries with post-partum data from the DHS data, the average coverage was 24.3% (Mukuria & Kothari 2007). Very limited repeat data shows an increase in Ghana from 28.3% to 43.0% and no change in Mali at 41.0% and 41.7%. In Tanzania coverage doubled from 10.9% to 20.1% whereas Egypt has increased coverage from 11.9% in 2000 to 37.5% in 2003 and 48.4% in 2005 (Mukuria & Kothari 2007).

While opportunities to administer supplements to women at delivery should be exploited, in many target countries, less than half of pregnant women deliver at home, and sometimes even less. Alternatively, mothers could receive their post-partum dose at the time of the newborn's first BCG immunization contact but less than a third do, even when there is good BCG coverage. This represents a missed opportunity to improve the vitamin A stores of deficient mothers and also to reinforce messages about the importance of early and exclusive breastfeeding for child survival. Recent studies in high HIV-prevalence countries may lead to a reduction in these programmes, at least in such environments (Fawzi 2006), and especially because efficacy has been hard to display in the impact on infants of women receiving them (Rice 2007).

Another challenge is the gap in national coverage that was due primarily to inadequate inventory management and supply forecasting. However, estimates for the most recent reporting year illustrate a promising reduction in the gap between availability and effective two-dose coverage. UNICEF and its partners are planning a review in the coming year to identify challenges and solutions to efficient capsule procurement, storage and management.

Donor support of vitamin A supplementation programmes has been critical to success so far, but additional resources will be needed if progress is to be sustained and accelerated. Governments will also need to assume responsibility and ownership of programming, as indicated by dedicated budgets for operational expenses and supplement supplies. Only one-third of priority countries currently contribute to supplementation through national budgets – primarily for operational expenses. A subset of ten of these countries has made initial plans to cover the full or partial costs of vitamin A supplements with national budgets, rather than relying on capsules donated via UNICEF from the Canadian Government through the MI. Nevertheless, the vitamin A supplementation approach has been positive experience and there is evidence of increasing sustainability by countries and on-going support from donors. Impact on mortality will now need to be demonstrated.

5.5.2 Iodine deficiency disorders

"Achieve sustainable elimination of iodine deficiency disorders by 2005…"

The iodine deficiency disorders since 2000 have been devilled by the fact that apparent prevalence from MICS and DHS appeared to plateau, or as one donor put it, 'flat-lined'. This has obvious implications for public health, IDD outcomes and donor enthusiasm. In fact, what is being measured is the number of households reporting using iodized salt and so is in fact a surrogate for the prevalence of the iodine deficiency disorders (IDD), although good correlation has been claimed (Mason et al. 2004). Measures of impact used total goitre rate until recently, despite acknowledgement that it is harder to assess goitre size accurately as programmes are underway, and it was not until the most recent WHO global database report that urinary iodine was used to measure adequate iodine nutrition on a global basis (WHO 2004). UNICEF and partners have reviewed indicators of sustainability such as production level, quality assurance and quality control and retail markets, and importation sites; outcome measures such as the proportion of households using adequately iodized salt (> 15ppm) (UNICEF 2007 websites such as http://www.unicef.org/sowc07/statistics/ statistics.php and http://www.childinfo.org); and for impact, the population iodine nutrition as urinary iodine levels (WHO 2007 website http://www.who.int/nutrition/topics/idd/en/index.html).The global database on the outcome of household use of iodized salt includes data from 117 countries, but as noted, the total denominator in different years are different as more countries are being added

(88 reported in 2002 to the UNGASS and 117 reported in SOWC 2007). There has also been a gradual shift from production level data to household and improved accuracy of salt testing kits. The current household data are based on nationwide surveys that are updated once every 5 to 10 years as new national surveys become available. The recently published database refers to the coverage in countries from studies from 1998 to 2005 (based on the results of the most recent survey available) (WHO 2004).

Table 5.7: Proportion of population, and number of individuals with insufficient iodine intake in school-aged children (6-12 years), and in the general population (all age groups) by WHO Region 2003 (WHO 2004).

WHO Region	Insufficient iodine intakes (UI<100µg/L)			
	School-aged children		General population	
	Proportion (%)	Total no. (millions)	Proportion (%)	Total no. (millions)
Africa	42.3	49.5	42.6	260.3
Americas	10.1	10.0	9.8	75.1
South-East Asia	39.9	95.6	39.8	624.0
Europe	59.9	42.2	56.9	435.5
E.Mediterranean	55.4	40.2	54.1	228.5
Western Pacific	26.2	48.0	24.0	365.3
Total	**36.5**	**285.4**	**35.2**	**1988.7**

As noted, current prevalence is expressed as adequacy of iodine nutrition based on median urinary iodine levels in school-children. As can be seen in Table 5.7, it was estimated in 2003 that 36.5% or 285.4 million children had insufficient iodine intakes (UI<100µg/L) (WHO 2004). This is expanded to the whole population to give 35.2% or 1,988.7 million people globally (WHO 2004). This translates into 72 countries with optimal or more iodine nutrition (5 are sufficiently high to risk adverse consequences). Another 40 are classified as having only mild iodine deficiency. Thirteen have moderate deficiencies and one severe, with 66 countries with no data (WHO 2004).

Besides the apparent plateauing of coverage, the WHO report in 2004 gave a total goitre prevalence/rate (TGP) showing a 4% increase in total goitre rate between 1993 and 2003, and a global figure of 15.8%, above the 5% cut-off point used to signify an IDD problem of public health significance (ICCIDD 2006). As ICCIDD have pointed out, this

is inconsistent with current iodine status based on urinary iodine and have offered several explanations (ICCIDD 2006). They note that: firstly, there is a time lag between the introduction of USI and the disappearance of goitre (Zimmermann et al. 2003) and that this time lag may be further increased when USI has been only partially implemented; secondly that 70% of the TGR prevalence surveys in the analysis period of 1993 to 2003 were carried out between 1993 and 1998 before the extensive introduction of USI programmes (WHO 2004); and thirdly, in areas affected by mild iodine deficiency, the sensitivity and specificity of TGP measured by palpation are poor (Zimmermann et al. 2000). Where analysis is restricted to surveys carried out in the last five years, total goitre prevalence is 28.9% lower than in 1993 (ICCIDD 2006). Similarly, the earlier report by the Micronutrient Initiative in the Food and Nutrition Bulletin had shown a decline in goitre prevalence, using different methods to account for the above factors, from 17.6% in 1994 to 14.4% in 2000 (Mason et al. 2004) (Table 5.3).

It is, however, likely some leveling did indeed happen, probably for several reasons: the initial coverage of the so-called 'low-hanging fruit' had been relatively easier e.g. countries with existing fortification, good infrastructure, increasing affluence and so on; the level of international effort declined somewhat in UNICEF and WHO after Jim Grant's (previous Executive Director of UNICEF and an active champion of USI) big push before the year 2000 deadline (and his untimely death) and also may have inflated some coverage figures from over-zealous offices; and thirdly, and perhaps most importantly, new countries were being counted and these had often come in later and with less developed infrastructures and hence coverage, so while the numbers were increasing the global average appeared static because of these many newly included, low performing countries. Finally, regional and global averages are population weighted; therefore the achievements and failures of many countries are masked by the highly populated countries. Related challenges, currently being assessed, are the increasing realization that the quality of iodized salt is now the next frontier, along with small salt producers and sustainability. In a country like India, which has seen marked increases in usage to over half of all households (after the earlier legal disputes on mandatory iodization) (see figure 5.17), it has been found by relatively small surveys by the MI, UNICEF and national partners, that the quality is below the recognized minimum of 15 ppm in about a third of all samples. The significant proportion of populations

using iodized salt at lower than 15 ppm are not reflected in published global data. Another issue will be that the remaining approximately 20% will be in populations that are harder to access, use other forms of salt such as rock salt (e.g. Tibet) and have large numbers of small salt producers for whom it has been harder to assure quality control or even ensure iodization in the first place.

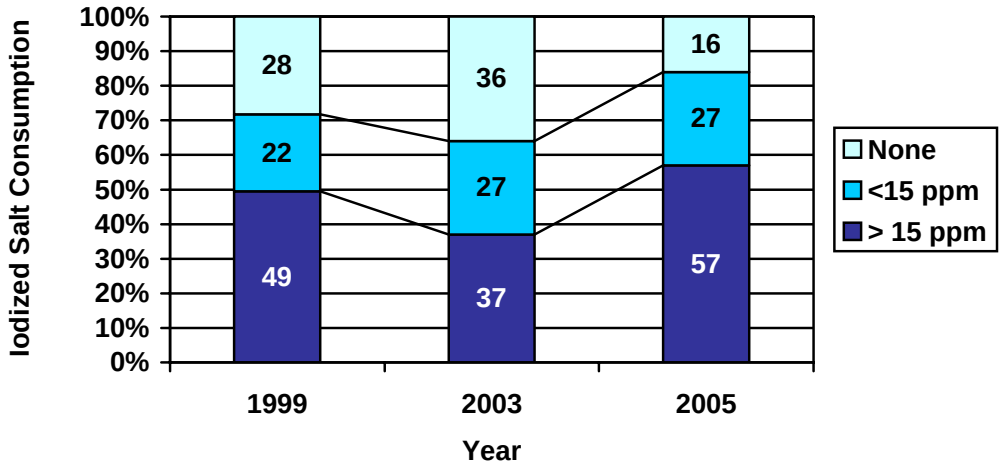


Figure 5.17: Universal salt iodization in India over three time periods (Mangasaryan 2007).

Consequently, iodine nutrition is still inadequate in 54 countries. Over one third (37%) of school-aged children globally (or 285 million) are iodine deficient while in the general population about two million persons remain iodine deficient and global goitre prevalence is 15.8%. On the positive side, when regions are looked at by country, over the last few years, many countries have made impressive progress with salt iodization, especially in South Asia and a surprisingly large number of African countries (Figures 5.18, 5.19 and 5.20).

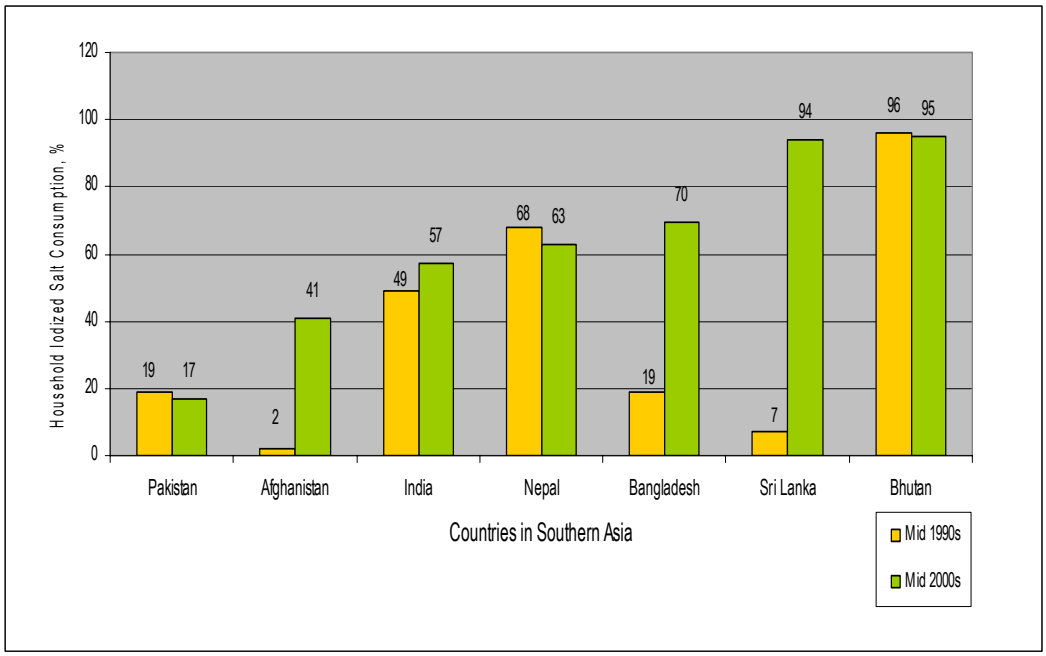


Figure 5.18: Improvements in iodized salt coverage in countries of South Asia from mid-1990s to mid 2000s (Mangasaryan 2006 based on UNICEF data).

The most recent figures show great improvement in salt iodization in the Africa Region with 64% of households reporting using iodized salt (54% in Eastern and Southern Africa and 72% in West & Central Africa) (Figures 5.19, 5.20), and for Asia but where India holds the regional (and global) figure back (South Asia has 51% coverage) but has improved (Figure 5.18). The good progress in CEE/CIS Eastern European countries in recent years is being held back to 50% by the Russian Federation and Ukraine which have so far chosen to rely on iodine supplementation to a large extent. East Asia and the Pacific, and Latin America and the Caribbean, regions demonstrate 84% and 85% coverage respectively. Nevertheless the global figure remains 68% for coverage of iodized salt (UNICEF not yet published in the UNICEF SOWC 2007) and the number of unprotected births estimated to be 38 million annually with 18 million of these births occurring in South Asia and 10 million in Sub-Saharan Africa (UNICEF SOWC 2007).

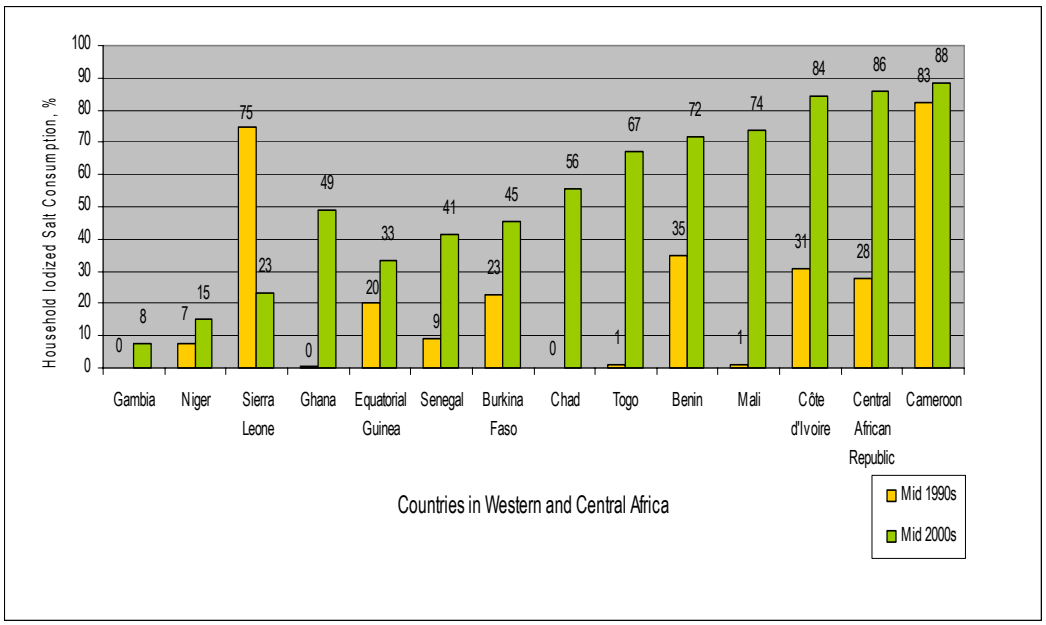


Figure 5.19: Improvements in iodized salt coverage in countries of West and Central Africa (Mangasaryan 2006 based on UNICEF data).

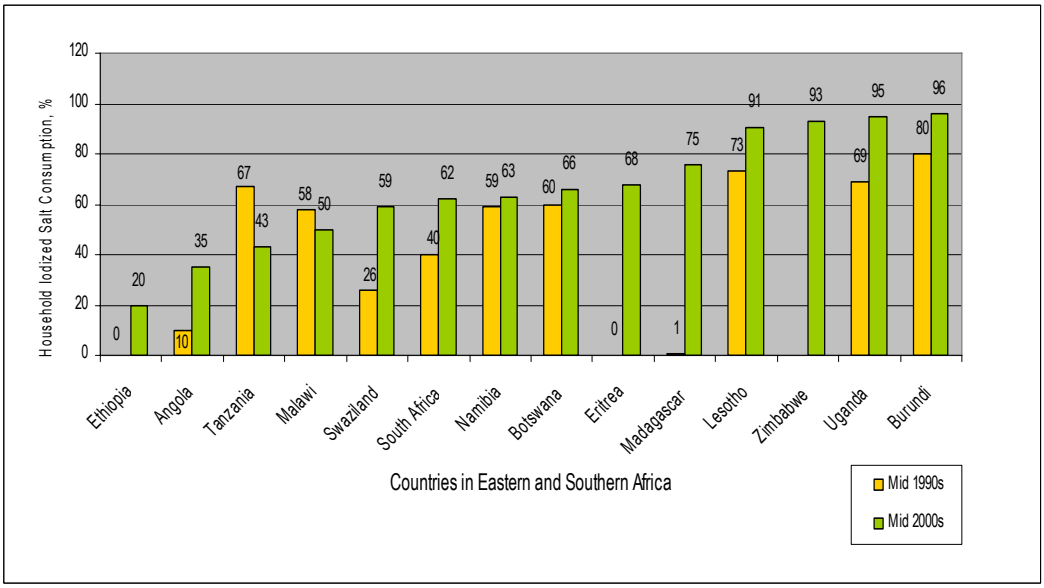


Figure 5.20: Improvements in iodized salt coverage in countries of Eastern and Southern Africa (Mangasaryan 2006 based on UNICEF data).

Moving ahead it is going to be important to address sustainability which will include attention to: (i) national ownership and leadership; (ii) adopted and enforced legislation; (iii) established monitoring systems; (iv) public-private partnership; and, (v) continued advocacy and public education (Mangasaryan & Untoro 2007). Other areas identified included:

- Legislation, continued enforcement, and monitoring systems - the strongest indicators of sustainable success;
- Salt iodization accepted by industry as a part of routine salt processing;
- Quality assurance/control systems at production/importation level;
- Communication – emphasizing the *exclusive* use of iodized salt;
- Business solutions in countries where a significant proportion of the population use salt from small-scale production; issues of affordability by the small producers and quality assurance;
- A special focus on highly populated countries which will also lead to improved regional and global indicators;
- Increased focus on adequacy of iodine levels by improving quality control of iodization to ensure appropriate levels at production and monitoring by household testing;
- Analysis of global trends based on country data and country trends rather than comparing regional and global rates annually.

Nevertheless, as can be seen in Figures 5.18, 5.19 and 5.20 the public health success story of universal salt iodization remains considerable and is expected to continue. Nearly 70% of the global population in the developing world now uses iodized salt (based on data from 88 countries). An estimated 3.8 billion people are now presumed to have adequate iodine nutrition, and 80 million newborn infants are estimated to be protected from brain damage related to iodine deficiency every year. At least 33 countries have reached the USI goal (90% of households consuming adequately iodized salt); at least 66 countries have more than 50% of households using adequately iodized salt, and of these, 27 countries are close to reaching the goal (70% to 90%). As of 2004 (based on urinary iodine levels) the number of countries with iodine deficiency is now 54 as compared with 110 in 1993, and of these 54 countries, 40 are only mildly deficient (WHO 2004).

5.5.3 Iron deficiency and anaemia

"…reduce by one third the prevalence of anemia, including iron deficiency, by 2010…"

Reports from both before 2000 (Mason et al. 2001, 2004, MI/UNICEF 2003) and since have reported little change in apparent prevalences in iron deficiency anaemia (McLean et al. 2007), although it is in fact usually anaemia that is being measured, such as in the DHS with portable 'hemocue' technology (Mukuria & Kothari 2007). The WHO Global database on anaemia gives updated national prevalences, but not regional or global figures. The global figure WHO gives on its website (of 37% with considerable inter-Regional variation) is based on data from 1990 to 1995 and was adapted from the 2001 publication (WHO 2001, WHO VMNIS 2007). Nevertheless, the trend data that are available show some very modest positive trends, although not apparently for pregnant women (Table 5.5).

However, in another later report, in a chapter in 'Nutritional Anemia' (Kraemer & Zimmermann 2007) by McLean et al. (2007) and based on the same WHO data that are given as national data by country on the WHO website, the global figure for non-pregnant women is 30.2% (c.f. 40.0% from the University of Tulane figures in 2000, and the earlier WHO figure of 35%). While this apparently does show some improvement, the authors emphasize that the two WHO prevalence figures should not be compared because of different methodologies used over the two different time periods and how the global prevalences were assessed. The conclusion is that the authors (from WHO but not yet published officially) doubt whether there has been any improvement (McLean et al. 2007). The global figures, disaggregated into three groups, give a prevalence of 47.4% (or 293.1 million) pre-school children with anaemia, 41.8% (or 56.4 million) pregnant women, and 30.2% (or 468.4 million) non-pregnant women, all of which certainly emphasize the size of the problem globally. What is an important change in these data is that for the first time it includes a national figure for China.

The interim WHO report notes that the global prevalence figures for similar groups in 1992 were 37%, 51% and 35%, for all women, and for pregnant and non-pregnant women respectively (McLean et al. 2007) (and which did include sub-national data for

China). Current estimates of 31%, 42% and 30% are therefore lower but the authors also noted that 'this change may be accounted for by the considerable difference in methods and coverage of national surveys' (McLean et al. 2007). One would hope the next time around, more effort will be made to make the figures comparative. The available DHS data since 2000 are not encouraging, with prevalences in sub-Saharan African children ranging from 69.4% to 91.2% (Mukuria & Kothari 2007). There were no repeat studies from that Continent and mixed or little change where there were repeat studies in children from other Regions e.g. in Egypt from 2000 to 2005 an apparent increase from 30.4% to 48.6%; an apparent decrease in Uzbekistan from 60.5% to 49.2%; and, little change in Bolivia (55.6% and 51.7%). The only repeat data in women were in Madagascar with no change (42.1% in 1997 and 46.0% in 2003/04) and Egypt again showing an increase from 27.6% in 2000 to 39.4% in 2005 (Mukuria & Kothari 2007).

Because anaemia affects vulnerable groups such as pregnant women and infants and children under two years, it needs to be addressed and tracked with increased effort. The increasing use (and recent inclusion in UNICEF's Supply Division, albeit for emergencies only at this point) of multimicronutrient powders, such as 'Sprinkles' offers another chance to reduce anaemias in infants and young children through 'home fortification'. The increased funding and efforts towards the control and prevention of malaria should also have an impact in endemic areas, although not a nutritional cause of anaemia as such. As also noted, suitable programmatic recommendations will need to be developed to ensure safe supplementation with iron to iron-deficient children in malaria-endemic areas. It is also quite likely that the emerging economic development, a growing middle class and documented changes in diets in countries such as China and India will be reflected in decreasing levels of anaemia, given it is so closely related to poverty. However, Ahmed has shown significant levels in the adolescent girls of relatively well-off families in Bangladesh, so social and behavioural factors well continue to need to be addressed (Ahmed 1999).

There are now far more national fortification of flour programmes with iron, folic acid and other B vitamins than ever before and improved bioavailability and quality of fortificants and one presumes this must be having an impact. Anaemia levels may also respond to the increased income for at least some in many economically improving societies,

through an increase in consumption of animal products, such as in South East Asia where the levels of anaemia have fallen in countries such as Thailand and Vietnam. In South Asia anaemia remains high and persistent for much of the population presumably due to low consumption of meat, and for reasons of poverty and cultural practice, as it does in much of Africa. The main challenge for anaemia prevention and control would seem to be to get the considerable economic impact of alleviating the deficiencies higher on policy makers' and funders' priorities of health problems that need to be urgently addressed.

5.5.4 Other micronutrients

"…and accelerate progress towards reduction of other micronutrient deficiencies, through dietary diversification, food fortification and supplementation…"

Little can be said about the other vitamins and minerals in terms of the recent trends in prevention and control of micronutrient malnutrition. The ones, apart from the major three public health micronutrients being largely discussed- vitamin A, iodine and iron, are zinc and folate deficiencies. Others of possible public health interest are vitamin B12, selenium and possibly other B vitamins such as thiamin in some areas. The interest in public health interest in vitamin B12 is currently largely as a response to the increasing national fortification programmes with folic acid and the likelihood, especially in countries like India, of masking vitamin B12 deficiency, which is likely to be high in countries with low animal food intakes due to cultural beliefs and poverty, and so also includes many African Continental diets. Selenium is of interest because of some evidence of a role in HIV transmission and is currently being investigated, and in the more recent past with its possible connection to Keshan Disease, Keshin-Beck Disease and Myxoedematous Endemic Cretinism which are all thought to be related to a deficiency in selenium. However there are virtually no global data on any of these deficiencies and they will not be further discussed but were reviewed by WHO in the 2004 publication with FAO (WHO/FAO 2004).

Zinc will undoubtedly be an important trace element in a public health sense in the coming few years and has a very active lobby as e.g. in IZiNCG (International Zinc Nutrition Consultative Group) which is encouraging WHO and UNICEF into recommending preventive zinc supplementation. Zinc supplementation is already

endorsed by the two Agencies as a therapeutic treatment for diarrhoea and there does appear to be evidence that it is likely to be a potential factor in reducing mortality and morbidity from both respiratory disease and diarrhoea (as is accepted by the forthcoming Lancet series on Nutrition). However, as seen earlier, it is difficult to diagnose, especially in terms of public health prevalence, although Hotz and Brown have estimated that maybe half of the developing world might be at risk, using extrapolations of likely dietary inadequacy (Hotz & Brown (2004). The WHO/FAO document does not hazard a guess at global prevalence (WHO/FAO 2004). Because there are currently no large scale programmes there are no estimates on trends of the possible deficiency. Consequently the zinc deficiency public health story will be told sometime in the future. Both UNICEF and WHO have indicated their resistance to another vertical programme and hence it is likely zinc programmes will continue to be limited to therapeutic use and multimicronutrient preparations, and fortification of staples.

Folate deficiency and its synthetic replacement, folic acid, is in a slightly different perspective from the other micronutrients in that much of the push is coming from the developed world as a measure against neural tube defects in new-borns, and increasingly as a possible factor in reducing cardiovascular disease (Wang et al. 2007) and possibly, depression (Taylor et al. 2004). The grain fortification lobbies such as FFI (Flour Fortification Initiative) are nonetheless encouraging its inclusion in flour fortification globally, along with iron and other B vitamins as an effective and cheap means of preventing neural tube defects and this is increasingly happening. Again, however, there are no figures for global prevalence (WHO/FAO 2004) and no trends apparent as yet, although increasingly, including very recently Australia, countries are including folic acid in their fortification programmes. Some questions remain about folic acid, including the long term effects of relatively high doses of folic acid as opposed to folate, and to its effects on morbidity and mortality in populations living in malaria-endemic areas, especially where the anti-malarials are folate antagonists. Again the story of folic acid as a public health intervention will become clearer over the next few years.

Finally the use of multimicronutrient formulations for children in the prevention and control of anaemia and for antenatal care in women and its relation to low birth weight are both currently developing an evidence base (SCN/WHO/UNICEF 2006). Many of

the efficacy trials have taken place for multiple micronutrient supplementation or 'home fortification' (Zlotkin & Tondeur 2007) but so far relatively few effectiveness trials. More of these will take place as WHO/WFP/UNICEF have published a statement on their use in infants, children and women in emergencies, and their use has already been evaluated in Indonesia after the Tsunami (de Pee et al. 2006).

5.6 Conclusion

The larger causes of micronutrient malnutrition, such as poverty, are often in common, as is apparent in global maps of prevalence, between the different deficiencies including underweight, and to this extent a tendency for their prevalences to move in parallel has been suggested by Underwood and others (IOM 1998). Poverty and the local environment (including water, sanitation, and access to health services) affect most forms of undernutrition, and improving such health ecologies might be expected to improve several deficiencies. On the other hand, iodine deficiency is sufficiently different in aetiology (while predominantly still affecting poor populations) that specific interventions for iodine deficiency will be most effective and access to iodized salt will be the major determinant of deficiency prevalence. Even with interventions against iodine deficiency there has been quite a lot of work on double (with iron) and triple (with iron and vitamin A) salt fortification but which has not really found traction on a larger scale. For vitamin A as well, as supplementation and fortification achieve increased coverage, rates of improvement in vitamin A deficiency may overtake those of, say, underweight. Mason notes that a relatively unexplored area is how far reducing specific limiting deficiencies may improve underweight, both directly for children and through maternal nutrition and birth weight (Mason, Helwig, Rivers 2005). Anaemia stands out as the most prevalent deficiency, very high in children as well as women.

The conclusions from all the above data and discussion largely mirror the conclusions of Borwankar, Sanghvi, Houston (2007) for the recent review leading to the development of the 10-Year Vitamin and Mineral Deficiencies Strategy being developed by all the relevant global agencies and partners (and currently coordinated by GAIN). Their conclusions have been adapted in light of the foregoing review of prevalence and trends.

- Apart from iodine, vitamin A and anaemia, there are insufficient data on the prevalence of other micronutrient deficiencies and so further surveys are needed to fill these gaps, although there is enough known already that programmes

should be scaling-up at the same time. Field methods for these three, and especially some of the ones of more recent interest, need to be developed, field-tested and applied.

- More evidence is needed on the relationship between interventions and different measures of micronutrient status as the present indicators have considerable limitations e.g. biological indicators are more invasive and cumbersome but more likely to be specific, whereas functional indicators are less specific.
- The deficiencies are caused by poor quality diets low in bio-available micronutrient content and by losses or poor absorption related to illness.
- Countries of sub-Saharan Africa and South Asia have the largest deficiency prevalence rates and the largest absolute numbers of micronutrient deficiencies but many countries from other regions are affected also, especially the more disadvantaged populations of those countries.
- Nevertheless, economic prosperity does not necessarily in itself protect communities or countries against deficiencies and special attention needs to be paid to the poorest, and especially to women and children.
- Deficiencies tend to cluster in households, communities and tend to be of more than one micronutrient at the time- this has programmatic implications.
- Global prevalences of vitamin A deficiency and the iodine deficiency disorders, particularly in their severe forms, have declined significantly as a result of large-scale programmes but which programmes need to be sustained or retained in high prevalence countries and areas.
- The prevalence of anaemia and iron deficiency remains high and suggests current programmes are ineffective. This is suggested to be because of the multiple causes of anaemia and the need to re-examine the paradigms of programming.
- The magnitude of zinc and folate deficiencies has largely been estimated indirectly and these estimates suggest that they are widely prevalent but as programmes are only starting recently, the prevalence has likely remained unchanged, except where diets have markedly improved through economic improvements.

The best data are for iodine, vitamin A and iron deficiency (or actually anaemia). However, where improvements have been seen because of societal change, it is likely

other aspects of the diet have also improved and hence the intake of other micronutrients. The public health reduction of the iodine deficiency disorders, measured both by impact and process indicators, has shown a remarkable success, as has the more severe manifestations of vitamin A deficiency (xerophthalmia) and probably vitamin A deficiency more broadly, with little discernable change at present on global levels of iron deficiency anaemia as measured by anaemia levels.

Overall, given the magnitude of the task, the programmes against micronutrient malnutrition should be considered a success, at least partly. Socio-economic improvement has played a large role in the biggest success stories e.g. South East Asia, and fortuitous, but imaginative opportunities, such as adding vitamin to national polio campaigns. Nevertheless the large amount of experience and serious investment by countries and donors has contributed strongly. The next chapter will then draw from these, factors that show a commonality and fall into facilitating and constraining factors.

Chapter Six

6.1 Discussion background

Before looking at the facilitating factors (promoters) and inhibiting factors (constraints), it may be helpful to have in mind four issues that impinge on success, or failure, and how to identify such factors. Firstly, the role of the many 'players' involved (as discussed in chapter four) and how they contribute to both success and failure; secondly, how exactly the two sets of factors can be identified in the absence of adequate studies (Mason et al. 2004a, 2004b); thirdly, how to distinguish the effects of interventions from underlying trends of improvement in the status of the general population; and fourthly, differentiation between programme specific factors such as what constitutes a successful fortification programme, compared with a higher level of what it takes to make any national programme successful.

It is not possible in most cases to do the sort of comparative studies desired by most epidemiologists and public policy makers, with true controls and, in many nutrition studies, double-blinded controls, although this has been done in some micronutrient studies. When a country has an established policy, it is usually unethical to do studies that do not provide at least what the government mandates e.g. if it is the policy for all children under 5 years to receive a vitamin A capsule twice a year, one cannot have a control group that is not getting at least this. Although not discussed further here, as such research methodology is outside the scope of the thesis, some intervention studies have used surrogate controls by arguing that as long as the intervention does not actively withhold or block the individual receiving the mandated intervention e.g. a child that would not have received a vitamin A supplement because of inadequacies in the current governmental delivery system, then it is ethical to include this child as control (understanding the fact that if the government system could be strengthened or improved, the child may well get a supplement). Another method has been to delay the introduction of an intervention, and to use those not yet receiving the intervention, as the control, or use of another micronutrient as the control e.g. iron/folic acid and/or vitamin A as was done in some studies on multimicronutrient supplementation to pregnant women

and its impact on low birthweight (Christian et al. 2003). A review of this study and ten other similar studies, organized by the author and others, by pooling and re-analyzing data, was unable to come to a definitive conclusion on the outcome of antenatal multimicronutrient supplementation, even though the mean birthweight was significantly increased and several micronutrient levels improved, partly because the numbers, though large, were not sufficiently powered in many cases to do so (SCN/WHO/UNICEF 2006). A further issue is the complication of nutrition effectiveness studies that require large numbers, extend over time, may be influenced by past nutritional history (even back to foetal experience), and are hard to control.

Consequently the observations in this chapter are drawn largely from descriptive and other observational and evaluation and monitoring studies. Victora and others have elegantly described the use of observational studies using adequacy or plausibility designs which are often the only feasible option in complex public health nutrition causal chains. In such cases and for evaluating large-scale interventions, as most micronutrient interventions are, usually at a national level, 'studies with plausibility designs are often the only feasible option and may provide valid evidence of impact' (Victora, Habicht, Bryce 2004). This chapter aims to bring together what information there is and analyze and group existing information by looking at reviews of programmes in countries which have been identified as successful and those that have had less success, and the factors suggested, and then to look for commonalities. As Mason has noted on impact of micronutrient programmes: 'micronutrient-deficiency control programs have been greatly extended at the national level in the last 10 to 15 years. However, rigorous evaluation of these is scarce, so that conclusions on impact are tentative and based mainly on indirect evidence' (Mason et al. 2004b).

Of course, the same factor can be facilitating or constraining, depending on the circumstances. For example, an authoritarian, centrally-planned government system can be a constraining effect if there is a policy not to encourage women's education, a known facilitating factor for better nutrition and health. On the other hand, such a government can legislate for a particular policy with relative ease e.g. that all wheat flour be fortified such as happened in Turkmenistan.

Both constraints and facilitating factors will be summarized, using the UNICEF Nutrition framework of basic, underlying and immediate factors (Figure 6.1) and by several matrices (Tables 6.1, 6.2, 6.3 and 6.4). As can be seen from the well-known figure, this looks at the final outcome of malnutrition and ill health through a series of increasingly proximal factors. The UNICEF Health and Nutrition Strategy, and the Ending Child Hunger and Undernutrition Strategy of the UN World Food Programme and UNICEF, in nutrition policy making and programming, extends this as they both reflect the importance of re-enforcing policy and programming at 4 levels: micro (village and community level); meso (district and subnational levels); macro (national); and, mega (global) (Gross personal communication 2004, Darnton-Hill, Kennedy et al. 2006).

In this chapter, facilitating factors are identified, then those likely to be inhibiting, and then the issue of sustainability is addressed, as the last is essential to any nutrition-related approach as, unlike immunizations, the intervention and policy needs are continuing, unless socio-economic, environmental and/or geo-political circumstances change markedly. Cost-effectiveness and cost-benefit are also discussed briefly given their impact on programme adoption, donor support and sustainability. At the conclusion of the fully-USAID funded OMNI (Opportunities for Micronutrient Interventions) Project, the author and his colleagues made one of the first attempts to analyze what works in effective micronutrient programming, and what does not (Darnton-Hill, Canova, Bolasny 1998). At the time, there was little experience to go on but some issues appeared to be emerging. However, the emphasis of that end-of-project report was on how to make the project successful within countries, but rather less directed at national, regional or global factors.

Since then, there have been several further efforts at this e.g. Allen & Gillespie (2001) reviewed the efficacy and effectiveness of nutrition interventions in general for the Asian Development Bank and the UN Standing Committee on Nutrition, with a view to answering ‘what works?’. More recently work, by the University of Tulane and the Micronutrient Initiative with other partners, only addressed countries in South Asia and South East Asia, and partially South Africa (Dietchler et al. 2004a,b, Mason et al. 2004a,b). However, the rigour with which it was done makes it very useful.

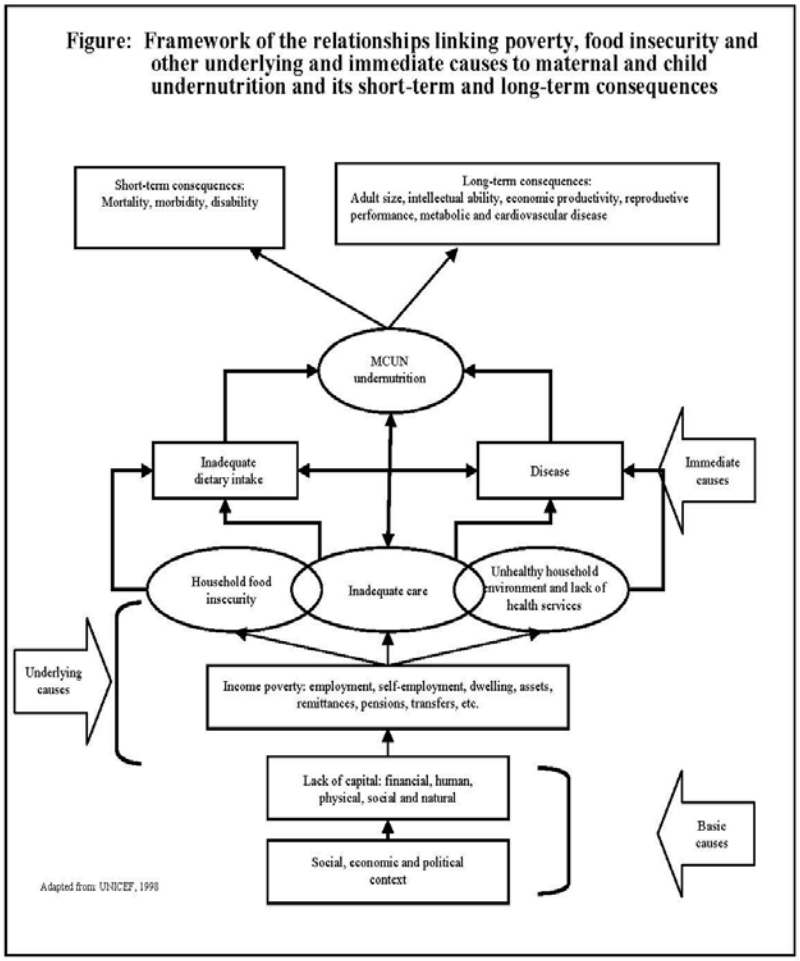


Figure 6.1: UNICEF framework of the relationship linking poverty, food insecurity and other underlying and intermediate causes of child and maternal undernutrition (UNICEF 1998 modified by Morris, Black and Victora 2006).

In the Allen and Gillespie review, although addressing nutrition in general, micronutrients constituted a good part of this, but again this excellent review was focused on Asian countries. A planned project, stimulated by Save the Children (UK), to identify what works and how to scale-up national nutrition programmes, specifically did not include micronutrient programmes, the rationale being that others are doing that, and that the

need was less acute (Anna Taylor, personal communication 2003). There is currently great interest in scaling-up vitamin A supplementation, and zinc supplementation, as part of child survival and development programmes, rather than as single, vertical programmes (Dalmiya, Palmer, Darnton-Hill 2006) and national effectiveness evaluation will be part of these efforts, including in the use of multiple micronutrients..

There have been more specific attempts addressing the specific interventions of supplementation (especially as the National Immunization Days are being phased out), fortification and dietary diversification (see Chapter 3). Less work has been done on evaluating impact (Mason et al. 2004a). As in the rest of the thesis, the emphasis will be on vitamin A (see Appendix 6.1), but a review of the literature showed that iodine programmes, especially USI, have been most extensively reviewed, with vitamin A a more distant second (although the author and others are currently doing this), and iron deficiency anaemia programmes, by far the least successful, inadequately assessed and evaluated. Apart from the recent global recommendations (WHO/UNICEF 2004) for the use of zinc supplements in diarrhoea treatment (and where supplies and logistics have been an early constraining issue), zinc programmes have not yet been implemented on a national scale anywhere. Similarly, multimicronutrient programmes have not yet been implemented at a national scale, although they have had extensive effectiveness trials and experience in emergencies e.g. in the Tsunami of 2005 (de Pee et al. 2006), and several Governments have preliminary plans to implement them for antenatal care. This does not exclude the experience of 'Western' countries, where half of some segments of the population take multimicronutrient supplements.

In the conclusion of the chapter, the experiences, including those from the author's personal experience, will be taken and sorted, and commonalities and degree of evidential support considered, in identifying the bare essentials that would appear to be necessary for successful programmes. Mason et al. (2004a) used a structure from their analysis of lessons learned that categorized the lessons by micronutrient: vitamin A, iodine and iron and further segmented the outcomes into factors affecting programme initiation, implementation and impact (Deitchler et al. 2004a, b, Mason et al. 2004b). Another common categorization has been to use the particular form of intervention such as dietary diversification, supplementation and fortification, with the last having the most information concerning programme implementation. However, in this chapter both

facilitating factors and constraints will be addressed under four levels of social organization/governance: micro, meso, macro and mega. From these, some factors that appear to be common to all will be expressed in a matrix for each; followed by cost issues and sustainability. Then, overarching factors will be addressed. One could argue that unsuccessful programmes are equally important to study, in terms of lessons learned, and perhaps more so in terms of constraints, and this chapter implicitly does that where the information is available, although unsuccessful experiences are likely to be less available in published reports. In the Appendix, is an application of identifying various factors for vitamin A programmes (Pak & Darnton-Hill, unpublished).

6.2 Facilitating factors

Facilitating factors and constraints are often the opposite sides of the same coin i.e. doing some action may facilitate the success of a programme, whereas not doing it may be a constraint. Consequently, active actions will be preferentially emphasized in both sections. They will be categorized, with some inevitable overlap, at the four major levels of governance: community and household (micro); subnational and district (meso); national (macro); and, global (mega).

6.2.1 Community/household (micro)

The ultimate success of a programme is when each household member has access to a dietary intake sufficiently adequate that his or her optimal micronutrient status is maintained. Obviously, where requirements are increased e.g. in high infectious disease load environments, this intake may need to be greater than for a healthy child growing up in a privileged and healthy environment. This is dependent not just on micronutrient delivery, whether through the diet or supplemented in some way, but also on the health and care of the child, and the environment in which he/she is growing (Figure 6.1). Increasingly more distal influences such as the mother's education and the global trade environment are recognized as reaching down to the village and having a potential nutrition and health impact on rural and urban children. Somewhat arbitrary distinctions will be made, especially according to delivery mechanism. So, for the community level, five areas will be briefly considered: food availability and accessibility; home gardening;

intrahousehold food distribution; health system availability; and, environmental issues including a lack of local conflict.

Food availability and accessibility

Food availability and accessibility were identified by the International Food Policy Research Institute (IFPRI) (Smith & Haddad 2000) as the main cause of children's undernutrition followed by female education, then women's status relative to men and then the health environment. These factors are important in micronutrient availability also. As earlier noted, the diets of the poor are characterized by poor quality and are micronutrient poor. Dietary improvement interventions to solve vitamin A deficiency have mainly focussed on improving the quality of the diet through enhancing accessibility and quality of food. In a review by Ruel (2001), she notes that dietary improvement interventions for increasing vitamin A and iron intakes have used a combination of actions, including: identifying foods with high vitamin A content and promoting their consumption; promoting income generating activities as an indirect way of improving supply of vitamin A rich foods; and, applying a behaviour change communication strategy to increase the level of knowledge and awareness of the beneficiaries (Ruel, 2001). Dietary improvement programmes largely differ from vitamin A supplementation or fortification in that beneficiaries are the major actors who make daily decisions on how to increase their own and their children's dietary intake of vitamin A through various means. Whereas vitamin A supplementation emphasizes "compliance" of beneficiaries as a facilitating factor to achieving high coverage rate, dietary improvement focuses on "empowerment", especially of women and low socio-economic populations (Ruel 2001, Bushamuka et al. 2005).

The home gardening programme that was initiated in Bangladesh as a small scale pilot program in 1988 by Helen Keller International (HKI) (Talukder et al. 2000, HKI 2004) had, in less than a decade, expanded into a large scale program, and was operated in 180 sub districts serving more than 700,000 households (now over 850,000). The key to its success was HKI's community level approach and its emphasis on sustainability, and by collaborating with local NGOs and encouraging the participation of women from the communities, the programme continued to expand without having to receive further input from HKI, other than technical assistance (programme management and planning of programme) (Bloem et al. 2001). In addition village nurseries, created by local NGOs

and community groups, played a major role in providing necessary resources, teaching healthy nutrition practices and various techniques for year-round gardening, and increasing the variety of fruits and vegetables. Community members were involved in designing, implementing, and evaluating the program. After one year of implementing a large scale program in 1997, the percentage of households without home gardens decreased from 25% to 2%, and the consumption of green leafy vegetables by children in households with developed home gardens was 1.6 times higher than the households that did not participate in the program. Moreover, fruits and vegetables produced from home gardening became a source of income. The positive impact on women's empowerment has been documented (Bushamuka et al. 2005). More recent modifications have included inclusion of animal sources in the diet and broader assessment of the approach (Bloem et al. 2001) as micronutrient intake can also be improved by targeting animal products to young children (Allen & Gillespie 2001, Murphy & Allen 2003), and has been shown to improve growth, cognitive and behavioural outcomes in children (Neumann et al. 2007).

Often home gardening programmes are coupled with nutritional education on how to choose and prepare micronutrient-rich food to increase the availability (Hotz & Gibson 2007), and other interventions such as the importance of breastfeeding (Pak & Darnton-Hill unpublished: Appendix 6.1). As consumers enter into the market system as suppliers, intra-household economic resources can be increased, resulting in better access to food and adequate dietary intake of vitamin A. Dietary improvement is more in line with the sustainable elimination of vitamin A deficiency and the broad nutrition and health enhancement status of children and women (Marsh 1998).

Intrahousehold food distribution

There is an extensive literature on this, especially from FAO (Ferro-Luzzi 2005), IFPRI (Haddad, Hoddindott, Alderman 1997), WFP (Webb, Coates, Weinberger 2001) and more recently from WHO (e.g. Webb, Nishida, Darnton-Hill 2007). Although most of the work has been done in total dietary energy and protein, where issues of female discrimination come into play, micronutrient status can be affected. On the whole though, it is more a problem of gender and culture and seems to have little impact on actual outcomes, except perhaps in South Asia (Darnton-Hill et al. 2005, Webb, Nishida, Darnton-Hill 2007).

Increasing the general availability and accessibility of micronutrient-rich food at the household level, as well as more generally as above, includes new technologies such as end-user fortification (e.g. 'Sprinkles') and complementary and other commercially available fortified foods (Neumann 2007, BASF undated, Zlotkin & Tondeur 2007) and in the future biofortification. Other social safety net interventions such as conditional cash transfers also seem promising.

Health system availability

This is extremely important, both in availability and accessibility and in the quality of services (UNDP 2003, UN Millennium Development Project 2005). As noted elsewhere, these are in disarray in many of the poorest populations- under-resourced and under-staffed, especially in sub-Saharan Africa (Chopra & Darnton-Hill 2006). Beyond noting their importance, they will not be further discussed here but are clearly critical e.g. when the micronutrient supplements are distributed through the Health System such as those containing iron/folic acid, vitamin A and/or zinc.

Environmental issues

In the IFPRI analysis, the surrogate measure used was for the health environment in particular and clearly is important. However, the broader threats to the global environment issue have finally come to the attention of policy makers as perhaps the ultimate determination of global health and well-being. Again, while critical, it will not be further discussed here except to note it is, yet again, the poorest populations that are likely to suffer first and most.

6.2.2 Subnational/provincial (meso)

Supplementation is a good example of a process needing all four levels- the supplement must reach the recipient at household level; the supplements must be in the local dispensary; the district must ensure adequate procurement; the national level must have a policy; and given the current CIDA-funded role of UNICEF and MI, there must be the timely movement of capsules around the world. However, because the main driver is at

the provincial level, even with National Immunization Days, supplementation will be considered here.

A recent analysis of twenty assessments of national vitamin A supplementation programmes by UNICEF and the Micronutrient Initiative (in which the author was involved) (MI/UNICEF 2004), aimed to identify the main bottlenecks preventing the achievement of high coverage of children under 5 years with vitamin A supplements twice a year in Africa and Asia. In the course of the analysis of the findings, key elements of successful programmes were grouped under policy, primary health care, awareness of beneficiaries, operational support and leadership and advocacy (Table 6.1).

Table 6.1: Common success factors for vitamin A supplementation programmes (MI/UNICEF 2004).

Policy	- Policy document with comprehensive set of policies for micronutrient malnutrition that include vitamin A deficiency - clear and comprehensive strategies with guidelines - effective communication - clear definition of nutrition 'essential package' including vitamin A supplementation
Primary Health Care	- Clear acknowledgment of role and active engagement of communities (resource people in the delivery of essential services - country is delivering (defined) essential package of services, with vitamin A being delivered bi-annually to at least 80% of the target population, including by 'mop-up' - (missed) opportunities maximally identified and addressed/used - rolling costed implementation plans for essential package developed with adequate resources allocated for vitamin A supplementation - a Government plan for increasing Government ownership of control of vitamin A funds
Awareness of beneficiaries	- Sufficient to motivate community members to seek vitamin A supplementation
Operational support	- training is consistent at all levels - regular, systematic, comprehensive, initial

	intensive and refresher training, then updating at other opportunities (why important, how to report and how to validate) - supervision as support and problem solving
Leadership and advocacy	- clear assignments of roles and accountability (to effect coordination) - vitamin A protection seen as a key component of national child survival and poverty alleviation

Vitamin A supplementation is being increasingly integrated into delivery of other health services (Dalmiya 2007), and iron with other micronutrients (de Pee et al. 2007). Delivery mechanisms are often poor, especially to the very poor, and novel approaches may well be needed such as the micro-encapsulated 'Sprinkles' and even a fortified fat-based spread such as RUFs (ready-to-use foods).

6.2.3 National (macro)

National activities such as policy, political commitment and legislation, and quality control and regulation all occur predominantly at a national level but like everything else will be strongly impacted upon by global forces and local infrastructures. Consequently, fortification fits most comfortably under the 'national' heading, as it is national commitment that appears to be most critical for success. It is also very important that countries have articulated national policies for all the micronutrients. Out of the 103 considered as vitamin A priority countries by MI and UNICEF, 47 have reported that they have adopted a nutrition policy that in almost all cases directly addresses vitamin A deficiency (excepting Malaysia which does not have a significant problem and Kiribati, which does). Eight additional countries have drafted policy and are awaiting their adoption and 13 do not have policies specific to nutrition but include nutrition and vitamin A in more comprehensive national plans for health, child health or immunization; 20 reported no national nutrition data and there were no data for 15 countries (Palmer personal communication 2006).

Fortification programmes

Up to this point, salt iodization has been the most successful fortification intervention, but with vitamin A fortification of sugar and of fats and oils, and fortification of cereals with iron and B vitamins as important in industrialized countries and in Latin America (Nestel 1993, Darnton-Hill 1998, Darnton-Hill, Mora et al. 1999, Darnton-Hill & Nalubola 2002, Dary & Mora 2002, FFI 2006, Dary 2007). From the experiences of successful fortification programmes, facilitating factors have been briefly summarized (Darnton-Hill 1998a), and re-affirmed and extended by Allen and Gillespie (2001), Mason's group (2004a, b, Deitchler et al. 2004a, b, WHO/UNICEF/ICCIDD 2001), and most recently by WHO and FAO (WHO/FAO 2006), as the following:

- Political will and support, which must be maintained from the development stage;
- Understanding of the problem by having adequate data on the magnitude of the nutritional problem being addressed;
- A consolidated database established with mandatory public reporting, including e.g. for IDD, regular monitoring on iodine status, and the use, supply, and quality of iodized salt and adequate data on food-consumption patterns;
- Industry support with early involvement of local industry and the private sector;
- Adequate technical expertise, proper testing under a range of real field conditions, and adequate training in fortification technology, quality assurance and control;
- A multi-sectoral approach in establishing a programme, including key governmental organizations, the scientific community, consumers, marketing specialists, and other relevant interested parties, early in the process; a national multi-sectoral; coalition/taskforce/council exists, meets, and is effective, including public, private and civil society members;
- Adequate application of legislation and regulations, including resources for effective enforcement (also to reduce supply and trade of non-iodized salt);
- Facilitative rather than punitive regulations i.e. guidelines should not be so restrictive as to impede the provision of high quality fortified foods nor hinder communication on fortification between relevant parties;
- Human resource training at the industry and marketing levels and of public health and food-safety personnel;

- Appropriate fortification levels evaluated and adjusted according to the bio-availability of the nutrient in the diets of the target population;
- Good bio-availability of the compound and no constraints on procurement of the micronutrients e.g. financial support for initial batch of fortificant;
- Intensive and appropriate investment in the information, education, and communication about the problem and the fortification approach, to raise consumer awareness and ensure consumer acceptability and also to ensure that there are no cultural or other objections against fortified foods;
- Minimal cost increase to the consumer, to the extent feasible;
- Relevant nutritional information available through adequate labeling to help ensure consumer involvement, commitment, and understanding of the advantages of fortifying foods.

To some extent building on the successful experience of vitamin A-fortified sugar in Central America and salt iodization (USI) (although not enough to achieve the overly optimistic UN World Fit For Children goal for elimination of IDD by 2005), strategies have been developed to ensure sustainability and achievement of USI in some of the remaining largest countries. As discussed in Chapter 3, the fortification of sugar with vitamin A in Central America has been a success story, as has, to a more limited extent, the fortification of margarine and other foods with vitamin A in the Philippines. There is currently a lot of activity in African countries and some in Asia on fortification of cooking oils with vitamin A also. Micronutrient fortification of cereal staples is especially important where these are major constituents of complementary foods (Allen & Gillespie 2001, BASF undated) and considerable progress is being made (FFI 2006, GAIN 2006). The Gates Foundation and USAID have both recently increased their support of GAIN (Global Alliance for Improved Nutrition) to promote fortified complementary foods with micronutrients for young children, beyond their core commitment of more general fortification which up-to-date has largely been iron and the B vitamins in vehicles such as flour, fish sauces and soya sauce.

6.2.4 Global (mega*)*

Global issues include those of trade laws (WTO 2003). There is a growing literature on the public health perspective of the trade-related aspects of intellectual property rights

(TRIPS) but which most concerns the current discussion because of the possibility of TRIPS being used to ban the import of fortified foods into countries which do not do so (irrespective of the epidemiologically defined needs of the populations). Despite assurances that public health issues would have priority, it has been upto the country wishing to not receive unfortified foods to prosecute the case, which many poor countries have neither the resources nor experience to do (Chopra, Galbraith, Darnton-Hill 2002). Another global perspective identified by Dietchler et al. (2004b) is interagency collaboration between national, local and international partners to ensure comprehensive planning, resource procurement and distribution, and information dissemination. It is important that, besides harmonization of trade laws and regulations, that donor bodies also harmonize both their expected outcomes with the country concerned and the monitoring requirements.

6.3 Programmatic facilitating issues

A relatively recent examination of programmes (not specifically those addressing micronutrient deficiencies) in resource-poor settings identified five assets of successful programmes, and barriers (see in the following section) (Berwick 2004). The assets were seen to be: consolidating and clarifying aims as an essential foundation for improving outcomes; using team-based improvement projects in direct care settings; building infrastructure, especially human resources and data systems; altering the policy environment; and spreading in stages (Berwick 2004). The last has a particular apposite example in Nepal where the use of Female Health Workers to deliver vitamin A capsules and other related health information, started in a few of the 52 Districts of Nepal, became sustainable in those, and then added more districts every year, until now virtually all the country is covered (Feidler 2000, 2001).

In their monograph, Allen and Gillespie (2001) aimed to identify programme success factors and identified seven factors without which programmatic success was considered to be less likely. The programme success factors identified were:
(i) the creation of awareness of the high prevalence, serious consequences and causes of malnutrition, including the hierarchy of immediate, underlying and basic causes, and the need to address causes at all three levels (as noted, the contention of the author is that four levels are essential i.e. including global policies);

(ii) the initiation, promotion and support of a process whereby individuals and communities participate in assessing the nutrition problem and decide on how to use their own and additional outside resources for actions;
(iii) clear identification and definition of time-bound goals (targets) at all levels of the programme/project. Young children from birth up to two to three years of age, pregnant and lactating women, and adolescent girls are usually the focus;
(iv) the identification and support of facilitators and community mobilizers, providing a sense of joint ownership of the programme/project by the community and the Government;
(v) good management of the programme project, including effective leadership, training and supervision of facilitators and mobilizers, an appropriate balance between top-down and bottom-up actions and effective community-based monitoring, and
(vi) the involvement of local NGOs, who often provide excellent facilitators as well as culture-relevant training. Where they were accountable to the community, this facilitated sustainability.

Coordination at all levels is consistently identified as necessary (Allen & Gillespie 2001, MI/UNICEF 2004, Mason et al. 2004a, UNICEF 2006a). A particular problem is the verticality of many micronutrient programmes so that e.g. vitamin A supplementation problem is the 'responsibility' of (and is therefore managed by) the national nutrition sector, but is implemented often by the EPI sector, usually as a result of the National Immunization Days for Polio Eradication (NIDs). UNICEF institutionalized this by having a major programme of 'Immunization+' where the plus includes vitamin A supplementation, and other interventions such as impregnated bednets for malaria prevention, deworming and so on. The 'plus' component was not infrequently either neglected or seen as of secondary importance (Darnton-Hill, personal observation 2004). There is an expressed concern that a similar thing may happen with vitamin A as an integral part of child survival activities, where it would become a commodity, but which conversely might impact on the sustainability of vitamin A supplementation-possibly either positively or negatively. Other related coordination issues includes relationship to IMCI programmes, and coordination between different elements of a vitamin deficiency prevention and control strategy so that food-based strategies, including fortification, are rarely coordinated with supplementation activities. This is also

often true of iron activities, and where there is iodine supplementation, of the activities to eliminate IDD.

Other studies have found similar issues (Darnton-Hill 1998b, Ahmed 1999, Rassas et al. 2004) and the reviews and analysis of Mason's group (Deitchler et al. 2004a, 2004b, Mason et al. 2004a, 2004b) who summarized their lessons learned, found that key steps taken in the initiation of national micronutrient-deficiency control programs were similar across study countries.

For *vitamin A supplementation programmes*, these steps were:

- National surveys documenting the extent of vitamin A deficiency in the country
- National workshops and advocacy meetings
- Establishment of national technical and inter-sectoral committees
- Securing assistance from bilateral and international agencies.

For *salt iodization programmes for IDD control*, they were:

- National surveys documenting the extent of the problem
- Establishment of national technical and inter-sectoral committees
- National workshops and advocacy meetings
- Securing assistance from bilateral and international agencies
- Integration of IDD control into national plan of action for nutrition
- Signing a decree mandating that salt for human consumption be iodized

And for *iron tablet distribution,* usually with folic acid, programmes:

- National surveys documenting the extent of iron deficiency (usually by low haemoglobin estimation) in the country
- Integration of the iron-deficiency control strategy into national plan of action for nutrition
- Development of a plan for programme implementation (presumably often with Maternal & Child Health, or other relevant, sectors)
- Securing of external assistance

Clearly there are common factors here. Where supported by other studies, these are listed in Summary Table 6.4. Interventions generally address only a single micronutrient and often only at one stage of the life cycle. The evidence is unclear whether a single nutrient approach is better or not. It may be that it is for some e.g. USI in IDD prevention and control. It may also be a matter of timing or programme implementation e.g. start off as single vertical programme at national level and then expand horizontally or in a more

integrated way e.g. Child Health Weeks (Dalmiya, Palmer, Darnton-Hill 2006, Dalmiya 2007).

Allen and Gillespie also identified five contextual factors important for successful national micronutrient implementation of programmes (Allen & Gillespie 2001). Political commitment at all levels of society was considered essential both for initiation and sustainability, including the integration of nutritional goals in development programmes- this is identified as a key factor in all the literature irrespective of the modality being used. Secondly: the involvement of women in decision making and hence the level of women's status and female literacy (Allen & Gillespie 2001, and also Quisumbing & Maluccio 2000, Smith et al. 2003,, Darnton-Hill et al. 2005). Thirdly: a good infrastructure for delivery of basic services, including committed and capable staff supported by community organizations such as women's groups, local NGOs and so on. Fourthly: charismatic community leaders with the ability and stature to mobilize and motivate people (Darnton-Hill 1998b, Allen & Gillespie 2001). And finally: the parallel implementation of poverty-reducing programmes (Allen & Gillespie 2001), a view more recently echoed by UNDP and the World Bank in their annual reports, and by the Millennium Development Project.

Information from the above reviews, along with many others (see references at the bottom of the Table) have been grouped and sorted to give the summary table of facilitating factors (Table 6.2).

Table 6.2: Identified facilitating factors to achieving the micronutrient UN goals

Social organization & governance level	**Intervention**	**Reference**
Micro (community, household and intrahousehold distribution)	-Use of community workers	b,i,l
	-Gender balance and intrahousehold distribution	
	-Home gardening	t
	-Diet e.g. animal products	a,b,f,j
	-Awareness of family and community members of problem, consequences and intervention	b,e,f,l
	-Local involvement of M&E with rapid feedback to users	f
	-Involvement of local NGOs	b
	-Minimizing of costs to poor communities and individuals in programmes	p,n,u

	-Attention to complementary feeding -Integrated approaches -Targetting -Time-bound targets	b p b, b,v
Meso (sub-national and provincial services)	-Decentralized health and nutrition services -Outreach (including 'mop-up' in national campaigns) -Adequate resources -Government plan disseminated and adopted -Training (at all levels) -Commodities and services at same time as training -Supervision & awareness by supervising health workers -Clear assignment of roles and accountabilities -M&E -Scaling-up in stages (time-bound) -Integrated approaches -Involvement of women -Charismatic local leaders (all levels) -Use of existing activities -Fixed annual schedules (esp. VAS)	 l l l.n.u f.l o b,l b,l l b,d,h,q l,p b,j,l f i
Macro (national policies and legislation)	- Use of existing activities e.g. NIDs - Policy document - Clear & comprehensive guidelines - Facilitating legislation - Regulatory actions - ENA - Coordination (at all levels) - National data available on problem - Donor support - Political will and support - Private sector support/involvement (esp. fortification) - Regular M&E - Targetting as appropriate - Parallel implementation of poverty reducing programmes/reduction in inequities	 d,f,g,k,l,s d,f,g,k,l,s f f c b,k,l f,g,l g,k b,f,n,u f,n,u f,g,k,u b,v b,r,s,v
Mega (global policies and frameworks)	- Trade policy incl. implementation of WTO policies when supportive of national public health interventions - 'Globalization' - Parallel implementation of poverty reducing programmes/reduction in inequities - Integrated approaches beyond just 'nutrition' - improved global delivery delivery and other systems - consistent policies - non-burdensome and consistent M&E	 b,r,s,v l l l,n,u

	(donor requirements) & - consistent indicators	l.n.o,u

(Akhter et al. 2006(a); Allen & Gillespie 2001(b); BASICS 2004(c); Berwick 2004(d); Bishai & Nalubola 2002(e); Darnton-Hill et al. 1998(g); Deitchler et al. 2004(h); Fiedler 2001(i); HKI/IPHN 2006(j); IFPRI 2001(s); Mason et al. 2004(l); MI/UNICEF (2003)(f); Network for the Sustainable Elimination of IDD undated(m); PMNCH 2005(t); Houston 2003(n); Sachs 2001(o); Talukder et al. 2000(q); UNICEF 1998(p); WHO/UNICEF/ICCIDD 2001 (k); World Bank 1994(r).

6.4 Inhibiting factors

As various writers have attempted to identify facilitating factors, they have inevitably also found situations and factors that are not conducive to success. For example, along with the facilitating factors, which he called 'assets', that Berwick (2004) identified in resource poor settings, were serious barriers. These he identified broadly as, firstly, 'politics' and the fact that political change cannot always be managed and that supportive officials may also suddenly change, requiring advocacy all over again. Secondly, infrastructures taken for granted elsewhere may just not be available, or functional. Unhelpful 'red tape' and bureaucratic obstacles are part of both of these. Thirdly, over-dependence on outside resources, including advice. Fourthly, travel throughout districts and rural areas. This last may well become more of a constraint in some settings as outreach and mop-up strategies are increasingly adopted as is happening in a post-National Immunization Days environment for vitamin A supplementation, but also child survival and immunization activities.

Leadership vacuums or simply the overload of too few trained people is a frequently cited issue. Others include language, roles, and finally 'scalability' or the potential of small, often successful programmes to be effectively scaled-up. The failure of the last has been seen all too often in nutrition projects, including micronutrient deficiencies programmes. As Berwick (2004) notes, as resource realities do not change quickly, that should be factored in right from the start, rather than models built under more ideal assumptions in central cities that do not reflect the contexts of much of the rest of the country (Berwick 2004). One might add cultural appropriateness where the beneficiaries are virtually always of a lower socio-economic status than the health care/supplementation deliverers, and may even be of a different cultural group or from

outside the area, or even outside the country, and who may be unfriendly and helpful to clients (Doherty et al. 2006).

6.4.1 Community/household

When synthesizing the lessons learned on programme implementation, Dietchler et al. (2004b) included some that were clearly inhibiting factors to be avoided as much as possible. Salt iodization was the most widely implemented (with remaining challenges of achieving national coverage and monitoring programme quality), with vitamin A programmes in most but not all study countries, and iron programmes in place in all the 11 countries but with varying coverage and limited evidence of effectiveness (Dietchler et al. 2004b). They noted a number of programme design and management principles associated with apparently effective implementation, including increasing demand by effective social mobilization and community participation, and by implication not increasing consumer knowledge and demand becomes a real barrier, especially in terms of sustainability.

A recent review of food fortification practices started as public health intervention programmes early in the 20th century in the United States concluded that the primary factor contributing to the long-term sustainability of food fortification is consumer awareness of the nutrient deficiency and consumer demand for and perceived benefits of the fortified food (Bishai & Nalubola 2002). All of the other reviews and many other programme planning documents emphasize that without community involvement of identifying the problems, planning to deal with them and a sense of ownership, including ownership of monitoring and evaluation, success is unlikely to be achieved in any sustained way.

6.4.2 Subnational/provincial

Dietchler et al (2004b) identified that strong programme management and motivation of programme staff at the local level are imperative, especially in supplementation programmes. In a strategic look at the IMCI programme, including the micronutrient aspects, Mason (2006) underlined the importance of having clear, systematic guidance for health workers so they can make a decision based on a clear set of well-defined instructions, with guidelines and materials adapted to the epidemiological, political and

local social environment (Mason 2006). Peeling (2006) also identified the need to have the programmatic tools available, including availability of micronutrient supplements (an emerging problem in the widespread adoption of zinc supplements for treatment of diarrhoea), at the same time as training.

6.4.3 National

Dietchler et al. (2004b) also identified a lack of well-developed institutional capacity for programme monitoring and evaluation as an important inhibiting factor. Part of this institutional lack can be reflected in what appears to be an inadequate capacity to evaluate proposed programmes and the likely national benefits, although apparent resistance to proposed new programming can reflect a perception that the proposal reflects donor priorities rather than national ones. Several cases from the author's experience are the following examples of national factors leading to an unsuccessful programmatic outcome.

An innovative approach to vitamin A deficiency in Bangladesh was tried in the late 1980s whereby a shellac, containing vitamin A, was to be sprayed on wheat coming in as aid wheat from the United States. Because wheat was much the less preferred staple, this had the added advantage of being indirectly targeted to the very poor, those in the vulnerable group feeding programme of the UN World Food Programme (WFP). Although it was a new technology, it was very extensively developed and tested and was technically feasible (Darnton-Hill 1988). After a great deal of effort, the proposed national intervention finally became untenable and politically unacceptable; partly it appeared because there was concern about a foreign power being involved in the food system, rumours about the fortificant (e.g. as a contraceptive agent), and it was also probably insensitively handled (Darnton-Hill 1988), resulting in the Government feeling it was being imposed on the country by USAID. Atta (ground wheat flour) may be fortified now, some 20 years later, through a partnership of WFP, USAID and the Government of Bangladesh and the millers with funding from GAIN, but several steps to making this a national programme remain.

A similar process occurred with vitamin A in monosodium glutamate (MSG) in Indonesia; again a combination of technology and politics led to this programme being stopped by the government after extensive laboratory work, efficacy trials, and a successful

effectiveness trial (Muhilal 1988). Although the microencapsulated vitamin A remained white in rigorous laboratory testing, when hanging in the sun in small cellophane packets outside the small rural *sarisari* shops, there was enough discolouration to concern the producer who sold MSG as the whitest of white products, and who had anyway been excluded from the early planning (Tjiong 1996). There was also some concern from professional medical associations and government about possible toxicity of MSG, although it is not classified as such by Codex Alimentarius. Similarly, the fortification of sugar with vitamin A in the Philippines did not go ahead when the world market price of sugar plummeted just a few months after the project launching in February of 1997, sending the sugar company into financial crisis and so it had to withdraw (Solon, personal communication), but is now being tried again. It is still relying on extensive external USAID funding and seems unlikely to succeed. In Zambia, in which USAID invested enormous sums of money to facilitate the fortification of sugar with vitamin A, while certainly not a failure, results are still awaited due to problems with private sector commitment, price of fortificant, and the considerable duty to be paid on the fortificant which the government has said it will lift, but has not yet done.

The recent analysis of twenty-one assessments of national vitamin A supplementation programmes (MI/UNICEF 2004), aimed to identify the main bottlenecks preventing the achievement of high coverage of children under 5 years with vitamin A supplements twice a year in Africa and Asia. The studies revealed significant problems at international and national levels, and that the status quo overall does not provide a viable basis for accelerating progress towards the high and sustained protection of vitamin A deficiency for all children under five years. In particular, while the integration of vitamin A supplementation with (routine) immunization contacts at fixed sites and via outreach does offer some scope for protecting infants, coverage is sub-optimal and children over one year-old are rarely protected adequately. This sub-optimal coverage is currently not being accurately assessed by current assessment of coverage that actually measures the supply side. Factors involved were identified by the MI/UNICEF (2004) analysis as being:

(i) The enabling environment is weak as the importance of vitamin A as a child survival strategy is imperfectly understood, inadequately championed and not specifically budgeted for at national level. Policy confusion and ineffective coordination are exacerbated by mixed messages from the international community about PHC and

child survival priorities. Insufficient collaboration and communication between the various global initiatives makes it worse and result in vitamin A supplementation programmes being fragmented, with absent or incomplete policy and leadership, limited strategic choices, and sub-optimal guidelines and coordination.

(ii) Secondly, gaps in capacity and training in key operational areas, including supervision, supply chain and logistics management, and monitoring, contribute significantly to low rates of coverage and protection.

(iii) Thirdly, the emphasis placed on tracking and measuring 'percentage coverage' alone tends to obscure the importance of action at all levels to assure the provision of full and sustained protection (i.e. high dose capsules at least twice a year) for each child under-five years of age.

With the iodization of salt in the Philippines, a monopoly was initially given by donor incentives and Government concurrence, to a single producer as a start-up incentive but who did not then produce the iodized salt as anticipated, and promised. Such special provisions given to one firm to encourage start-up action, can distort incentives for other companies, as happened in this case, when the concession of an extended monopoly effectively inhibited competitors from also fortifying salt. The national Parliament of India recently repealed legislation that mandated universal iodization of salt, thus turning a success story into a potential failure. This hinged on arguments of personal rights of access to non-iodized salt, and underlines the importance of consumer education and political will. Some Indian States then planned to enact their own legislation to enable iodization. However, as was the case with the Cantons of Switzerland (Bürgi 1998), some States were considerably more pro-active about doing this than others. Since then the National Parliament has repealed the legislation that did not mandate universal salt iodization, at least for human consumption, but now a further appeal against this has further delayed national adoption. With all fortification, there is concern about the leakage of non-fortified (and hence usually cheaper) foods across borders e.g. leakage of non-iodized salt across borders in Africa. Some apparent success stories, such as the iodization of salt in Eritrea and its export to neighbouring countries, collapsed under the pressure of the conflict with Ethiopia. Another such reverse occurred in Sierra Leone, where iodized salt coverage declined from 75% to 8% in 1999 due to the civil war (ICCIDD 2000b).

Similarly in the Russian Federation and Ukraine, where severe IDD had been largely eliminated by effective control measures as early as the 1940s and 1960s, government programmes were discontinued in 1970. After the dissolution of the USSR in 1991, IDD became again a common problem in nearly all the Newly Independent States (Gerasimov 1998). Dary sees such reversals (although he was referring to sugar fortified with vitamin A) as a continuing tension between the needs of 'free trade' and 'public health', and that legislative tools may be insufficient without reliable enforcement mechanisms and consumer awareness (Dary 2001).

It has become apparent that constraining factors in non-sustained programmes in developing countries include the lack of consumer demand due to non-recognition of any likely benefits to come from consuming fortified foods or taking supplements, as well as the lack of public sector policy makers' recognition of the nutrient deficiencies as a public health problem. The importance of advocacy at the political level as well as raising consumer awareness regarding the magnitude and effects of the nutrient deficiency, and the role of fortification as a complementary approach to other interventions, need to be recognized as prerequisites for success (MI/UNICEF 2003). Ignoring these factors has been shown to contribute to the failure of programmes. Nevertheless, even with the best social marketing, price can remain a constraint. In very poor households, there is very little price elasticity, and even a minimal increase can discourage the buying of fortified foods. In a study in South Kalimantan and South Sulawesi in Indonesia, it was found that while instant noodles were consumed in nearly all households in both areas, consumption of fortified noodles was related to socio-economic status and was lowest among farmers and share croppers, who might well be some of those most at risk (Melse-Boonstra et al. 2000).

Among others, two articles have identified constraints in IDD elimination: one promising to show how to avoid the 'seven deadly sins in confronting endemic iodine deficiency' (Dunn 1996), and the other promising to show how to fill 'common potholes in the salt iodization road' (Joost & Locatelli-Rossi 2003). Noting the pledge in 1990 by most countries of the world and the international agencies to eliminate the iodine deficiency disorders, and that the technology for the assessment and implementation is sufficient to attain this goal, Dunn (1996) listed seven potential barriers: (i) unreliable assessment of iodine deficiency; (ii) poor iodine supplementation plan; (iii) exclusion of relevant

stakeholders who should include health authorities, other arms of Government, the Salt Industry, Health professionals and academics; and the iodine poor community itself; (iv) inadequate education at all levels, from Government to affected populations; (v) insufficient monitoring with public reporting of the results; (vi) inattention to cost of fortification which should be perceived to be apportioned fairly by all parties; and, (vii) non-sustainability which will not happen without (v) and (vi) especially (Dunn 1996). He expands on them all but number (ii), poor iodine supplementation plan is probably most relevant where the author notes that iodized salt is the preferred supplement and that its effective application frequently requires extensive changes in salt production and marketing, and that poor handling of these changes will endanger the iodization programme. He also notes that other measures include iodized oil, iodized water and iodine drops, all of which are useful but that the long range solution should generally be iodized salt, which was also a decision made in early 1990s by UNICEF. Supplementation with iodized oil or in other ways, is being reconsidered in emergency situations, very hard to reach populations and maybe in pregnancy (WHO 2007, Untoro et al. 2007).

The potholes identified by Joost & Locatelli-Rossi (2003) are similar but emphasize technical barriers to the actual iodization such as insufficient knowledge of IDD among salt producers, small, informal rural salt production, household use of non-iodized agricultural salt, informal repackaging, and use of coarse salt. They also note that these do not occur just in low income countries, citing the use of iodized household salt varying from around 10% in Australia and Belgium and 20% in the much of the Baltics to almost 90% in some Latin American and Caribbean countries (Jooste & Locatelli-Rossi 2003). Nevertheless, many countries in Africa also have high levels, including 90% coverage in Nigeria and with a continental average of 70% (UNICEF 2006b). The fact that European countries still have a public health problem has recently been emphasized by a report from WHO by the author and others (Andersson et al. in press).

When synthesizing lessons learned on programme implementation, Dietchler et al. (2004b) also included inadequate public knowledge of programme services and inadequate promotion of public motivation- and this has been particularly true of supplementation services but also of fortification. In iron programmes poor coverage has been linked to poor compliance through forgetfulness, fear of difficult delivery, and side

effects of the supplement (Dietchler et al. 2004b). Fear of increasing the amount of blood and hence risk of maternal haemorrhage has been reported anecdotally to the author in both Indonesia and Zambia, by both recipients and, more worryingly, health workers. Galloway & McGuire (1994) argue that it is more often the logistics of getting the supplements to the women in an acceptable form that are the main constraints. However, it seems most likely to be a combination of both (WHO/UNICEF/UNU 2001, Darnton-Hill, Paragas, Cavalli-Sforza 2007). Knowledge and motivation of health-care workers were, not surprisingly, also identified as important intermediate factors by Dietchler et al. (2004b). Too much reliance on single interventions was also identified as a constraint, suggesting the need for more multi-facetted strategies. Post-partum supplementation with vitamin A is generally less well-established than young child programmes- this is also true in Africa (MI/UNICEF 2004. Rice (2007) largely because, besides a more recently implemented intervention, there is often poor utilization of antenatal care services and relative infrequency of births in health facilities (Rice 2007). Iron supplementation remains the least well implemented for many of the same reasons: poor routine health care coverage, low access and utilization by women, especially rural women, inadequate availability at the local level and poor compliance.

Allen & Gillespie (2001) considered the following conclusions to be supported by nutrition intervention trials. Among the constraints (although not identified as such) were: that in most developing countries, the micronutrient content of unfortified complementary foods is inadequate to meet infant requirements, so that it is particularly difficult for infants to consume enough iron, zinc, or calcium in their early diets. Other micronutrients at potential risk are vitamin A, riboflavin, thiamin, and vitamins B6 and B12. Addressing single micronutrient deficiencies would seem therefore to be less efficient but currently the evidence base for interventions with single micronutrients is stronger and has been conclusively shown for vitamin A, iron, zinc, iodine and vitamin B12 (Allen & Gillespie 2001). Considerable work is now underway investigating both the effectiveness and efficacy of multimicronutrients interventions (SCN/WHO/UNICEF 2006), especially in HIV-endemic populations.

6.4.4 Global /Transnational

Dietchler et al. (2004b) identified poor interagency collaboration between national, local and international partners that failed to ensure comprehensive planning, resource procurement and distribution and information dissemination. They might have added the role that donors could play to facilitate this process. Donors have been essential in micronutrient programmes, especially Australia, Canada, the Netherlands and the USA, as well Belgium and Germany in parts of Africa- both in the initiation, and technical and financial support and their role has recently been reviewed again. Among the conclusions were that, while very important to micronutrient programmes, there are major funding and programmatic gaps and a lack of coordination (Phillips & Mattos 2007). Conversely, this role, especially of the Development Banks, should not be underplayed as a major factor that has sometimes impaired access to the very poor, and sometimes been a constraint in sustainability. The World Bank's structural readjustment policies are now considered to have set back health and education programmes for the poor in much of Africa. Pushing user pay health systems has arguably removed basic health care from the reach of many of the poor with women likely to be especially disadvantaged. The geo-political systems currently in place, especially for trade, are also currently a major constraint, especially for the very poor, and there is a considerable literature on this (e.g. Chopra & Darnton-Hill 2006). It is not further considered here, as there appears to be a limit to how this can be mitigated, and it is somewhat beyond the scope of this thesis. However, many other recommendations that are frequently made, will be unable to have their planned impact without concomitant political change. This is sometimes addressed, especially by USAID-funded proposals, as efforts to improve 'good governance' within the country. While undoubtedly important, there is frequently little communities and the targeted poor can do about this, especially without tacit or direct support from donor countries.

Although the private sector has long played a major role in fortification e.g. salt, margarine and oils, breakfast cereals and the like, in more affluent countries, they are only now being seen as an essential partner in the developing world. While both the public and private sectors will continue to have somewhat different agenda and roles, sustainability, at least in fortification, will not be ensured without an active partnership

with the private sector. A role for the private sector at village and town level shops and stores in delivering iron and folic acid supplements is being tested in several countries, and actively promoted by several of the donors. Conversely these 'partners' often have differing ideas of what are the desired and likely outcomes (Richter 2003) and more thought and clarity needs to be addressed up-front if expectations are not to be disappointed.

As noted in Chapter Four, the sectors most often involved consist of national governments, international and multilateral agencies, international consultative groups, bilateral agencies, international NGOs/PVOs, national NGOs, individuals, and increasingly, the private sector. The interactions that seem likely to achieve most, especially in fortification, are those of the public and private sectors working together (Darnton-Hill 1997, 1998a, 1999, 2000). It is also the most controversial. A much vaunted 'public/private partnership' was the one between UNICEF, USAID and others, and the multinational Roche pharmaceutical company (the last being, at the time, one of the two main global suppliers of vitamin A and other micronutrients, both as supplements and fortificants) which took a beating, although a surprisingly mild one, when it became clear that the two companies had been systematically defrauding 'partners', including national governments. They were subsequently fined some millions of dollars, but some years later are on the GAIN Board. They have since spun off the micronutrients commodities provision activities to a newly formed company. In this context, it is to be noted that the World Trade Organization (WTO) has had to explicitly bring in clauses to protect public health interventions that may be at risk from over-zealous interpretation of the 'free trade' provisions (WTO 2003, Oliveira et al. 2004). Similarly the World Bank now states without reservation that 'globalization' while overall advantageous, has not been good for the very poor (World Bank 2006, Chopra & Darnton-Hill 2006). Others would argue this is because the globalization process continues to be corrupted by the very countries promoting it (Pinstrup-Andersen, personal communication 2006).

Nevertheless, by the very multi-sectoral nature of the problem, the most successful approaches are likely to be those crossing boundaries. Although part of the immediate success of micronutrient programmes appears to have been their vertical, top-down approach, there is some evidence that without community involvement that success is unlikely to be sustained (Allen & Gillespie 2001). As seen with the experience of IDD,

even in Europe, commitment by governments is critical (Andersson et al. in press). When this has been unsure, or unpredictable, the sustainability of the programme is lost, and a whole generation may suffer the consequences (Bloem, de Pee, Darnton-Hill 2004). At this point, the NGO sector comes in to particular strength. However, there has been a temptation by some bilaterals, in particular USAID, and some NGOs/PVOs, to bypass local authorities or national governments, and set up parallel delivery systems. This may give better short-term results, and may be ethically defensible when a minority group is being by-passed by official channels, or even when regular services are totally inadequate due to lack of resources or adequate trained personnel. Nevertheless, it is not a recipe for longer-term sustainability, especially when external funding stops. As in structural re-adjustment, and debt obligations, one of the reasons there are inadequate resources for public health nutrition programmes are due to geopolitical forces, not infrequently global policies endorsed and exploited by the same donor countries that are providing the bilateral aid (Sachs 2001).

Most countries continue to be dependent upon external donors such as CIDA and UNICEF for vitamin A capsules, iodine and other fortificants. A top priority was therefore seen by Dietchler et al. (2004b), reflecting a major inhibiting factor, as building national governmental, industrial and academic capacity for programme implementation and management. Particularly in resource-poor countries, the conflicting demands and agendas of multiple donors can cause major difficulties. Donors need to beware of inappropriate interventions given primary health care limitations and the need to get real involvement and feedback that can acted upon by the workers and the social, economic and technical context (Peeling 2006, Chopra & Darnton-Hill 2006).

Table 6.3: Identified constraints to achieving the micronutrient UN goals

Social organization & governance	**Intervention**	**Reference**
Micro (community, household and intrahousehold distribution)	- Lack of coordination with other programmes - Lack of resources - Dysfunctional health (& other) systems - Failure to increase consumer demand - Cultural insensitivity - Gender balance and intrahousehold distribution - Price increases	q,t, v y i t h j,n,p

	- Fear of side effects and other lack of consumer and health worker knowledge - Infant feeding constraints (traditional weaning foods, lack of fortified complementary foods - Lack of outreach/inaccessibility	i q,u
Meso (sub-national and provincial services)	- Decentralized health and nutrition services - Difficulties in internal travel - Lack of communication between health workers and community - Poor staff motivation - Lack of strong programme management	 d f i b,i
Macro (national policies and legislation)	- Lack of infrastructure - Lack of capacity/poor planning - Parallel programmes/too much reliance on a single programme - Poor governance incl. lack of priorities, corruption, inconsistency* - National strife - Lack of Government support (all levels) - Lack of facilitating legislation (esp. fortification) - Regulatory actions 'red tape' - Over-dependence on external funding - Lack of resource realism - Lack of scalability - Lack of institutional capacity - Failure to get early involvement of other partners (e.g. private sector in fortification) - Lack of data on problem (or recognition of it) - Lack of consensus on effects of deficiencies - Poor M&E	d d,aa b,i d b,q aa,n,q d d d d i,o,q,aa n,q,r,aa h,q,aa n,q,r,z
Mega (global policies and frameworks)	- Trade policy/WTO - 'Globalization' - Poor governance incl. lack of priorities, corruption, inconsistency because of * changing administrations with changing priorities - Donor policies - Inadequate attention to cultural, national sensibilities - Strife, proxy wars - Lack of coordination in legislation In sufficient collaboration between various global initiatives	 f h d,h,i,t d,h,i,t t q q

(Akhter et al. 2006(a); Allen & Gillespie 2001(b); BASICS 2004(c); Berwick 2004 (d); Bishai & Nalubola 2002(e); Doherty et al. 2006(f); Dalmiya, Palmer, Darnton-Hill 2006(g); Darnton-Hill et

al. 1998(h); Deitchler et al. 2004(i); Dunn 1996(j); Fiedler 2001(k); HKI/IPHN 2006(l); Houston 2003(m); IFPRI 2001(n) Joost & Locatelli-Rossi 2003(0); Mason et al. 2004 (p); Melse-Boonstra 2000(q); MI/UNICEF 2003(r); Nestel 1993(s); Network for the Sustainable Elimination of IDD undated(t); Peeling, Heyman, Mason 2006(u); PMNCH 2005(v); Sachs 2000(w); Talukder et al.2000(x); World Bank 1994(y); UNICEF 1998(z); WHO/UNICEF/ICCIDD 2001(aa))

Given the above evidence, the constraints might be regrouped to apply to all micronutrient programmes using a framework originally used for fortification (Darnton-Hill 1998a modified from Micronutrient Initiative 1997).

- Technical constraints: installation and maintenance of necessary supply logistics and hardware, e.g. maintenance of fortification machinery; suitability of supplements such as vitamin A capsules (e.g. capsules contained porcine elements in earlier versions); quality and stability of multimicronutrient powders and risk of cross reactions among constituent vitamins and minerals; and so on;
- Decent quality of iron tablets for compliance, stability of fortificants under the sub-optimal distribution and storage conditions traditionally found in developing countries; and the development of new cost-effective fortificants and ways of delivering micronutrients;
- Socio-economic constraints: the targeted groups are often those with least purchasing power; price of initial batch of supplements or fortificant and capital costs, and the demand on foreign exchange;
- Infrastructural constraints: poor distribution systems due to poor infrastructure; limited experience of inter-sectoral coordination; and frequent changes of government; lack of access to commercially-processed food and accessibility to supplements limited by geography, poverty or cultural preferences;
- Political constraints: political support may be lacking due to perceived priority of other health and nutrition interventions and lack of awareness of the magnitude of problems and benefits of addressing it; lack of facilitating legislation and a lack of equal opportunities for all potential participating companies;
- Other implementation constraints: weak quality assurance systems at the private sector level; ineffective enforcement of any existing regulations at the public sector level; and a lack of proper monitoring and evaluation of the programme and, therefore, limited intermediate corrective follow-up measures;
- Perhaps the greatest potential constraint is who bears the added cost e.g. different Government sectors; cost of improving health and other systems; and for fortification,

to the millers, the added cost is the sum of premix, equipment amortization, labour and quality control. To these must be added advocacy, social marketing, increased public awareness, monitoring and effectiveness of quality assurance, and someone must pay for all this, however small the actual amount per person.

6.5 Sustainability

Three factors have been identified as essential for sustainability: efficacy, appropriateness, and demonstrated feasibility (IOM 1998). In the same report from the U.S. Institute of Biology of the Academy of Science, the authors point out that sustainability has two components: process- the continuity of a successful intervention; and outcomes- continuation of a significant, positive impact on the intended beneficiaries. Pharmaceutical supplementation is of proven efficacy but effectiveness over time remains a challenge for public health micronutrient programmes. Nevertheless, supplementation with iron, especially for pregnant women, and probably infants, had for a long period no alternative, and is of confirmed efficacy, although 'it has proven ineffective in practice in most developing countries' (Viteri 1997). There has been increased emphasis on fortification and other forms of supplementation e.g. multiple micronutrient powders for home fortification such as 'sprinkles' (Zlotkin & Tondeur 2007), on the assumption that commercial fortification has an in-built sustainability and that social marketing of multimicronutrients will prove feasible (Cavalli-Sforza et al. 2005). However, in both cases the very poor, the very disadvantaged and the very remote are likely to need special programmes, probably delivered through Government or NGO systems.

The Indonesian vitamin A programme is one excellent example of an intervention that evolved over a 20-year period from 100% donor support to the current programme, which is entirely funded by government monies (Reddy 1989, IOM 1998). More than half of countries (57%) reporting vitamin A supplementation programmes in 2004 were contributing to operational costs and a growing number are procuring at least a portion of their own capsules (12 in the most recent ordering cycle in 2006) (Dalmiya, Palmer, Darnton-Hill 2006). Significant advocacy efforts, particularly in Eastern and Southern Africa, have also led to the inclusion of vitamin A supplementation in poverty reduction strategies and sector-wide approaches (Dalmiya, Palmer, Darnton-Hill 2006). Vitamin A supplementation has been in existence as a public health intervention for over 30 years

e.g. India (Reddy 1989). In countries with pockets of vitamin A deficiency as a public health problem, and for iron, supplementation will be required for many years yet, but methods of targeting, enhancing delivery, ensuring supplies, encouraging demand and compliance will continue to need to be streamlined and adapted to local circumstances. Although vitamin A supplements are currently being purchased or donated through UNICEF by the Canadian Government through the Micronutrient Initiative, this cannot continue indefinitely, although a parallel to the continuing need for immunization in countries' EPI programmes can be made.

High coverage of vitamin A capsules were achieved by adding vitamin A capsule distribution to the Polio National Immunization Days (NIDs), even in countries with poor health systems (UNICEF 1998, Goodman et al. 2000). The need for a follow-up day on which a second vitamin A capsule can be given six months later, was an issue but it turned out that the experience with Child Health Days (or a variety of other names but reflecting a national campaign approach every 6 months) has been useful in the post-NID phase, as discussed below. Building on their established two periods during the year, it was largely successfully handled, with so far good sustainability in Bangladesh (National Vitamin A Weeks); 2 days in April and October in Nepal using the Female Community Health Volunteers- again with >80% coverage sustained over three years; and, the *Araw ng Sangkap Pinoy* on World Food Day in the Philippines that has also had over 80% coverage, although that later dropped from 88% to 78%, with concerns of fatigue (HKI, unpublished). Constraints are seen as health worker fatigue with the campaign approach, lack of supplies on the day, and need for continued promotion and greater consumer demand.

Now however, polio NIDs are steadily being phased out, as polio persists in only limited areas. Meanwhile perceptions of campaign style approaches as involving unsustainably high (human and financial resource) costs are widespread (MI/UNICEF 2004). Although vitamin A supplementation has been carried out for decades in some countries, systematic scaling-up in the context of child survival programming began in the late 1990s, so that in recent years there has been a renewed commitment to vitamin A supplementation programmes and an increasing focus on achieving universal coverage as part of UNICEF's integrated health and nutrition strategy (UNICEF 2006a), largely informed by the Lancet child survival series (Jones et al. 2003).

Maintaining high vitamin A supplementation coverage has been more successful than imagined (Dalmiya, Palmer, Darnton-Hill 2006), even in some of the most challenging countries of the world such as Niger where it has occurred since 1997, when the country became one of the first countries in Africa to successfully add vitamin A supplementation to the Stop Polio National Immunization Days (Aguayo et al. 2005, Aguayo & Baker 2005). The challenge mentioned above of the second dose led in 1999 to the first ever National Micronutrient Days (NMDs) in Africa, and since 1999, the combination of NIDs and NMDs has ensured that over 80% of targeted children have received two doses annually (Aguayo et al. 2005). The authors attribute this to five factors; leadership and ownership by the Ministry of Public Health; district level planning and implementation; effective training and flexible delivery mechanisms; effective social information, communication and mobilization; and, responsiveness and flexibility of the Ministry and other partners (Aguayo et al. 2005).

The analysis by Aguayo and Baker (2005) of 11 sub-Saharan countries showed that in the absence of effective and sustained policies and programmes for the control of vitamin A deficiency, an estimated 42.4% of children 0-59 months of age were at risk for vitamin A deficiency. Broad vitamin A programme action and effective and sustained policy would bring about 25% reduction in mortality compared to 1995 mortality levels (i.e. before the large-scale supplementation programmes in these countries). They concluded that a stronger political commitment and a more appropriate level of investment in the effective control of vitamin A deficiency could make a large contribution toward the reduction of child mortality (MDG4) (Aguayo & Baker 2005).

To address issues of cost and sustainability, there is increased interest in using a more targeted approach to supplementation through health care facilities, and other channels likely to reach groups at risk, including using the private sector e.g. iron/folic acid (Cavalli-Sforza et al. 2005), and the recent success of NIDs being accompanied by vitamin A supplementation (Aguayo et al. 2005). Dalmiya (2007) and colleagues have recently reviewed the effectiveness of using Child Health Weeks in three countries in Africa (Ethiopia, Tanzania and Uganda) and found that they are achieving sustained high coverage of child survival interventions, including vitamin A supplements.

Nutrition education and increased knowledge of both consumers and policy makers are seen as an integral part in the sustainability of any program. However, the beneficial impact of nutrition education on micronutrient status has not been well documented in the past, except for limited efforts to increase consumption of food sources of β-carotenes e.g. in Thailand (Smitasiri et al. 1993). Analyses of both the Bangladesh and Vietnam experience show that the reduction in vitamin A deficiency in those countries has been mainly an effect of the vitamin A capsule supplementation programme, and that the underlying cause of lack of vitamin A in the diet (through fortification or through foods in the diet) has still not been solved (Bloem, de Pee, Darnton-Hill 1998). Again, it would appear that complementary approaches of nutrition education, fortification, dietary diversification, and where needed supplementation, together are most likely to ensure sustainability.

Mason et al. (2004a) found, as have others, that there was too much reliance (in their Asian sample but likely would hold elsewhere) on single interventions and that more multifaceted strategies are needed, although Gwatkin (2006) has recently questioned this assumption in relation to IMCI not reaching the very poor. Particularly for vitamin A and iron, the sustainability or even effectiveness of supplementation alone in permanently reducing the deficiency 'is open to some doubt' (Dietchler et al 2004b) but, high coverage is being achieved in over 57 countries (Dalmiya, Palmer, Darnton-Hill 2006) and has been in existence for over 30 years in several South Asian countries. Ideally, sustainable reduction of deficiency is seen to depend on improved nutrient intakes through diet, which requires promotion of dietary change, including increasing micronutrient content by fortification. Many countries report concern reflecting this and it has been suggested that medium-term planning incorporate mechanisms to promote technical, financial and organizational sustainability of such food-based programmes (Bloem et al. 2001).

Although vitamin A supplementation coverage is quite high when compared with other nutrition interventions e.g. iron supplementation for young children, attaining the goal of universal coverage presents significant challenges. Only a few countries have dedicated delivery mechanisms to sustain even current levels of coverage with most relying on annual or semi-annual planning. Reaching remaining children, usually the most disadvantaged, will require further effort still, both in terms of planning and likely

expenditure (Dalmiya, Palmer, Darnton-Hill 2006). A key barrier to sustainable programming remains the lack of policy recognition of the benefits of vitamin A supplementation. While opportunistic linkages with other interventions produced high coverage, minimal efforts have been made to effectively communicate the importance of vitamin A for child survival. Knowledge, attitude and practice surveys have revealed this information gap at all levels, from consumers through policymakers (Dalmiya, Palmer, Darnton-Hill 2006), and until addressed, the transition from a push to demand driven intervention, as necessary for sustainability, will not happen. This is critical at the policy level. Generous support of the Canadian government has largely driven progress, and continued investment will be necessary in the medium-term for external technical assistance; however, it is time for countries to assume some of the costs of vitamin A supplementation through health and child survival budgets, if real sustainability is to be achieved, and this appears to be happening (although has not been explicitly encouraged by the donor).

Examining national programmes in some detail has often been helpful, as an earlier study of Bangladesh's programme by Ahmed showed (Ahmed 1999) where he also suggested recommendations for improvement. Fiedler (2000) has done something similar for Nepal, and Rassas et al. in Ghana (Rassas et al. 2004). In his comparative look at 3 supplementation programmes on countries in three different Continents, Houston (2003) notes that "these supplementation programmes have not competed with other efforts to improve vitamin A status- in fact for each; dietary means are stressed, including fortified foods. In Nepal, Female Community Health Volunteers bring examples of vitamin A rich foods, and they may become involved with addressing vitamin A deficiency in pregnant women. In Ghana, awareness is done hand-in-hand with discussions of vitamin A rich foods. (Houston 2003). "It appears likely that these supplementation programs are sustainable. In Zambia, fortification of sugar may play an increasing role…' and while modifications for each programme may be made, supplementation is likely to be needed for some time. Supplementation programmes do however need to move from being a quick short-term solution to being an integral part of Government preventive Services (Houston 2003). Costs for a minimum package of activities to sustain high coverage are small considering the improvement in mortality (Houston 2003).

Recent experience with the Global Fund to fight AIDS, Tuberculosis and Malaria suggests an emerging different view of sustainability, relying on sustained international assistance and not on present or future self-financing (Ooms, Derderian, Melody 2006). This has long been the view of IVACG, comparing it to immunization (Sommer, personal communication 2000), and now Médicins sans Frontières. This prolonged sustainability by external support has been likened to a form of World Health Insurance (Ooms, Derderian, Melody 2006). Nevertheless the past 20 years have shown many examples of faltering enthusiasm by donor countries over time for specific programmes (including for a while immunization), when coverage dropped markedly; or in a change of priorities, and so it would seem prudent for countries to fund their own supplies as they become able to. Without doubt, if Canadian CIDA changed its policy tomorrow, many countries' vitamin A programmes would abruptly cease to exist.

6.6 Monitoring and evaluation as a critical factor in the sustainability of micronutrient programmes

Inadequate capacity for monitoring and evaluation is recognized as a major liability in most programmes (Deitchler et al. 2004b). As noted by Mason et al. (2004b) rigorous evaluation of micronutrient control programmes, despite their expansion, is scarce.

Given the role of vitamin A supplementation coverage as a proxy for programme impact and an internationally agreed-upon indicator of progress towards child survival goals, strengthening monitoring at all levels is a central part of moving forward. A recent meeting of implementing partners, held in New York on 19-20 July 2007, set forth a vision for strengthening VAS coverage monitoring. Although partners agreed that it is not currently feasible to directly measure two-dose coverage as per guidelines, a modified set of indicators was recommended that would facilitate the indirect estimation of children fully protected (Dalmiya, Palmer, Darnton-Hill 2006). Coverage will be reported separately for infants 6-11 months, children 12-59 months reached during the first semester of the year (whether through distinct events or routine) and children 12-59 months reached during the second semester. In addition, partners called for the systematic recording of vitamin A supplementation on child health cards regardless of delivery strategy. Better documentation in this new era of child health packages will enable improved coverage monitoring through existing survey efforts. Finally, a

framework is under development to inform country self-assessments of programme sustainability (Dalmiya, Palmer, Darnton-Hill 2006).

For fortification, monitoring includes measures taken by the private and public sectors to assure that the food is fortified at adequate levels and properly labeled when it reaches the consumer. A good monitoring system needs specific mechanisms for prompt corrective actions to be taken by relevant parties when problems are identified. Evaluation includes identifying patterns of consumer behaviour in terms of the purchase and consumption of the fortified food; determining intake of the nutrient of interest and the contribution of the fortified food to this intake (in the case of multiple micronutrient fortification, one nutrient may be chosen as an indicator); and impact on the public health problem being addressed. As discussed earlier, few programmes have been properly evaluated and impact on public health determined, although some successful programmes have been shown to have had the intended health benefits. Despite economic constraints, evaluation should be given more emphasis in the design and implementation of fortification. It has been shown that demonstrating the public health benefits of fortification programmes is critical in long-term sustainability and in gaining the commitment of public and private sectors as well as consumer demand for the fortified food (Darnton-Hill 1998a, Bishai & Nalubola 2002, Mora & Nestel 2000).

Surveillance systems set up to observe trends of the prevalence of the public health problem over time help evaluate the impact of fortification as well as other intervention programmes. For example, in the US it has been identified that iodine levels may have needed to be reduced, largely because people were getting iodine from other sources e.g. in bread and when iodophors have been used to clean cow's udders, as was also the case in Tasmania 20 years ago. Urinary iodine was measured in NHANES I (1970-74), and found to be higher than desirable, which prompted bans on some iodophors and adoption of alternatives for iodine in dairy operations. However, the median concentration decreased more than 50% between 1971-74 and 1988-94 (NHANES III). These findings, although not indicative of iodine deficiency in the overall US population, were considered to define a trend that needed monitoring (Hollowell et al. 1998). Recent evidence from Australia and New Zealand has shown the re-emergence of mild to moderate iodine deficiency (Eastman 2006). In European countries, lack of adequate attention by government and other factors has meant iodine levels have at times decreased in countries after fortification had been in place in for many years (Andersson

et al. in press). Germany, after the adoption of the 'principles of voluntary action' following reunification (Meng & Schindler 1998) and in Switzerland, where to correct for falling levels of urinary iodine, it was decided to raise the salt iodine to 20-30ppm in 1998 (Bürgi 1998). Europe has had fortification for over 70 years now, and still has not achieved true sustainability, as evidenced in the rising rates of IDD in the eastern Block countries (Gerasimov 1998), and as in the examples of Germany and Switzerland.

Nevertheless, theoretical concerns continue to be of concern when a programme is being started. Sometimes these are real concerns, which is where monitoring is essential. In Zimbabwe, and later in PR Congo, there were several reports of salt fortification with iodine in communities with chronic iodine deficiency leading to potentially fatal cases of Jodbasedow or iodine induced hyperthyroidism (IIH) disease (Delange et al. 1999; ICCIDD 2000). These were found to be due to poor or absent monitoring and sudden introduction of overly fortified salt coming in from surrounding countries (Todd & Dunn 1995). A more theoretical possibility is iron overload, especially in Caucasian men suffering from a tendency to haemochromatosis, but with the exception of massive amounts of iron in locally brewed beer in south and east Africa, this does not appear to be a real concern in developing countries where iron deficiency is widespread (Harvey et al. 1999).

6.7 Cost-effectiveness, cost-benefit and sustainability

A figure often quoted is that of the World Bank 1993 document that not addressing micronutrient malnutrition will cause a country a loss of up to 3% GNP, whereas the cost of addressing the problem is only 0.5% (World Bank 1994). The way in which these figures came about is not entirely clear but they have been widely, and effectively, used for advocacy. In making the economic case for investment in Nutrition, Hoddinott of IFPRI (2007) cited such arguments as better nourished people impose fewer health-related costs on society; improved nutrition contributes to wealth creation to the extent that it is causally linked to the development of skills (such as cognitive skills) that underpin development; and that the benefit:cost ratio for investments in improving nutrition are high (also Mason, Musgrove, Habicht 2003 and Behrman, Alderman, Hoddindott 2004). Hoddindott cites the impact on physical and cognitive function of iodine and iron deficiencies, as well as prolonged undernutrition diminishing psychomotor and fine motor skills. Vitamin A and zinc and other micronutrient

deficiencies such as those of folate have considerable other child mortality, morbidity and health care cost burdens as has been demonstrated in earlier chapters. It is not only children that bear the costs as e.g. anaemia increases the risk of maternal deaths and undernutrition decreases wages of workers (e.g. studies from Brazil), and reduces productivity (e.g. by 5% in Indian manual labourers) (cited by Hoddinott 2007). He also notes that overall costs can be very large such as in China, India and Indonesia where micronutrient deficiencies have been estimated to be costing $US5 billion, $US2.5 million and $US0.75 billion respectively (MI/UNICEF 2003, Hoddinott 2006, Alderman & Horton 2007).

With the widespread use of DALYs (Disability-Adjusted Life Years) by WHO and the World Bank, attempts were made to establish the cost of effectiveness of micronutrient interventions compared with others such as immunization (WHO 2002). In these early estimations (which are being continuously updated by WHO and others and will be included in a Lancet nutrition series scheduled to be published in late 2007), micronutrient interventions came out relatively well for vitamin supplementation, especially vitamin A supplementation and iron interventions, as did universal salt iodization. This approach explicitly reflected the prominence of economic rationalization, including in overseas development aid, and the need for interventions to show their cost-effectiveness e.g. by cost per death averted for each intervention (Rassas et al. 2004). There has long been a 'traditional rationale for investing funds in nutrition activities because doing so was considered intrinsically a good thing to do' (Hoddinott 2007). For over a decade now there have been repeated and on-going attempts to demonstrate that investing in nutrition activities, and especially micronutrient activities, is also good economics (Levin et al. 1993, Mason, Musgrove, Habicht 2003, Behrman, Alderman, Hoddindott 2004, Hunt 2005). However, except for some key personnel in some bilateral funding agencies, especially CIDA and USAID, this has not been widely accepted, or certainly not adequately financially supported, despite widespread academic and policy endorsement e.g. the Copenhagen Consensus of an international team of economists (Copenhagen Consensus 2004). Particularly this has been true of iron despite having perhaps the strongest economic case (Ross & Horton 1998, MI/UNICEF 2003, Baltussen, Knai, Sharan 2004, Copenhagen Consensus 2004, Hunt 2005, Alderman & Horton 2007).

These many efforts tried also to compare across the different micronutrient interventions, as well as determining the actual cost, however difficult this is to do in reality. Generally vitamin A came out quite well, as did universal iodization of salt. Several attempts were also made to compare different interventions for the same micronutrient (Sanghvi 1993). In these comparisons, food-based approaches (excluding fortification) appeared to come out worst compared to supplementation and fortification (Sanghvi 1993). Implementation policies were implicitly affected by such calculations. For example, despite home gardening being an important source of vitamin A in the diets of the poor in Bangladesh (Bloem et al. 1996), such food-based approaches are regularly seen as a highly priced intervention, and hence rarely a first-line option. It has been argued that this result is partly because longer-term benefits such as women's empowerment by having a small independent income from, e.g., home gardening are generally not captured. These benefits include those such as increased use of health services by women, increased and earlier taking of sick children for treatment and increased expenditure for children on food and education (Marsh 1998, Bloem et al. 2000, Bushamuka et al. 2005, Darnton-Hill et al. 2005).

However these cost-effectiveness studies became increasingly complex and expensive. Earlier estimates by Levin et al. (1993) and calculations used in the PROFILES package developed with support by USAID were used to advocate for nutrition, including micronutrient, interventions in health policy (Darnton-Hill, Canova, Bolasny 1998, MI/UNICEF 2003). Ambitious attempts for vitamin A have been attempted in Ghana (Rassas et al 2004), Nepal (Fiedler 2001) and Zambia (Houston 2003, Rassas et al. 2003). Often in response to donor requests, estimates have been made of the cost of a supplement delivered, cost of death averted, total numbers of lives saved by an intervention and so on. These are clearly very dependent on assumptions made, especially perhaps in estimating the number of 'lives saved' but a figure much sought after by donors e.g. in the estimates of cost per death averted in Ghana by vitamin A supplementation, which ranged from $US77 to $US277 and up to $US586 for total programme costs (Rassas et al. 2004). There is currently some criticism of the underlying assumptions, e.g. by attributing too much impact from one dose of a 200,000 IU supplement (based on advice from Johns Hopkins University, West personal communication 1994), as opposed to the necessary same dose 2 to 3 times a year. Similarly, in estimating the cost of delivering a supplement which depends not only on

local conditions but also on source of supplements and on assumptions relating to use of staff doing other tasks besides delivering micronutrients, training and health system infrastructure (Fiedler 2001, Fiedler, Saunders, Sanghvi 2007).

Programmes for the control of any micronutrient deficiency are worthwhile, in health economics terms, only if the cost of the programme is lower than the benefits which result from the correction of the deficiency. Cost-effectiveness of an approach is defined as the cost of achieving some specified outcome, in this case, the cost of averting each case of a particular micronutrient deficiency. While sometimes expressed in terms of cost per death-averted, this is a less useful calculation for iron supplementation or iodine fortification, where effects on mortality are less well-documented, and the important benefits include increased productivity instead (Andersson et al, in press). The key economic effects are assumed to be brain damage in infants. Cost-effectiveness is especially useful when comparing different programmes with the same outcome, but is less useful in the design of IDD control and prevention programmes because there is broad consensus on the intervention of choice, salt iodization (USI) (WHO/UNICEF/ICCIDD 2001).

Cost-benefit is where the monetary cost of an intervention is compared to the monetary value of the outcomes or benefits (Andersson et al., in press). In this case the benefits are increased productivity and reduced health costs and the other costs of caring for those damaged by micronutrient deficiency. Cost-benefit estimations are useful for advocacy for increased resources and to compare health and nutrition interventions to the many other kinds of government spending (Fiedler 2000). In calculating cost-benefit ratio, the proximate health intervention outcome, such as reduction in the prevalence of xerophthalmia or goitre, or change in mean serum retinol or urinary iodine excretion levels of the population, has to be converted to a financial outcome, usually derived from other studies. In the case of USI, past studies that looked at the cost of productivity loss per birth to a mother with iodine deficiency, have been used to estimate the cost of one person removed from goitre (as an intermediate outcome) (Andersson et al., in press).

More recently, WHO has looked at the cost-effectiveness and benefit-cost ratios of micronutrient interventions, especially fortification (WHO/FAO 2006). Salt iodization

programmes were again found to have 'very high cost-benefit ratios'. If the costs of iodine fortification are $0.10 per person per year (Mason 2004b), then the benefit: cost ratio of iodine fortification is about 40:1. If the costs are as low as $0.01 per person per year, as suggested for Central America (Dary cited in WHO/FAO 2006), then the programmes will have a considerably increased benefit: cost ratio of something like 400:1. The Copenhagen Consensus found micronutrient interventions (it remains slightly unclear exactly what sort but likely iron supplementation) to be the second most cost-effective intervention (Lomberg 2005, Copenhagen Consensus 2006).

There has been some extensive work by USAID micronutrient projects (OMNI, MOST) on this (Darnton-Hill, Canova, Bolasny 1998, Houston 2003) but conclusions seem very much dependant on country and methods used, especially what to include in the costs and what are existing costs of the Health (usually) system. Clearer estimates would also help some understanding of the longer term resources needed to sustain high coverage. Houston reported on cost studies done in Ghana, Nepal and Zambia (Houston 2003). The average annual cost per child dosed is $0.25 in Ghana and $0.67 in Nepal which compare very favourably with earlier estimates such as $1.42 in Peru and $3.25 in Guatemala (quoted in Houston 2003). He notes that the figures for Ghana and Nepal are programme specific costs (in year 2000 prices) and did not include shared Government personnel and capital costs (Houston 2003). Despite the wide range of estimates, and costs per child, the vitamin A supplementation programmes are often quoted to be 'highly cost-effective relative to many other public health care interventions' (Rassas et al. 2004, Ahmed & Darnton-Hill 2004), and as noted, the Copenhagen Consensus and other groups have found this to be generally true of micronutrient interventions. Which leaves the bigger question of why this has been difficult to 'sell' to donors and Governments?

Involvement of the private sector in the fortification of processed, commercial foods with multiple micronutrients, such as noodles, is being increasingly tried in affected, non-OECD countries. It is likely country Governments will also be more involved with the private sector in the sale of supplements, following successful implementation of such programmes in Lao PDR, Philippines and Vietnam (Cavalli-Sforza et al. 2005). A recent survey in the Philippines found that while around 90% said they would be willing to buy supplements most would not spend more than 20 pesos (about 5 US cents) on

iodized oil or vitamin A supplements, citing a lack of money and a feeling that it was the government's responsibility (DOH/HKI, personal communication 1998).

Studies have shown that fortification is both cost-effective (i.e. it has advantages over other methods as a way of increasing iodine intake, with evidence less clear for vitamin A, zinc and iron although the last has been in place in countries such as the USA, and parts of Latin America for over 50 years), and has a high benefit-cost ratio (i.e. is a good health investment) (WHO/FAO 2006). Past studies, all now somewhat dated, and taken from different national settings, have attempted to compare the cost-effectiveness of iodized oil injections in Bangladesh, Indonesia, Peru and Zaire (14-46 1986 US cents), with water fortification in Italy (0.04 mid-1980s US cents) and salt fortification in India (0.02-0.04 cents as reported in 1996 cents) (Hetzel & Pandav 1997, Mills 1983 and Levin et al. 1990 cited in a WHO review for which the author was a consultant (Andersson et al., in press)). However, for iodine, on a large public health perspective, USI is the most cost-effective and sustainable (Hetzel 2004, Eastman 2006).

The social benefits of the elimination of micronutrient deficiencies have been less extensively evaluated, partly because they are less easy to cost but are likely to be significant. The benefits of the elimination of IDD, on the basis of reviews of data collected from several regions of the world: Bolivia, Ecuador, Germany, India, including Sikkim, and the United States of America (Levin et al. 1993, Hetzel & Pandav 1997, Hunt 2000, Kahaly & Dietlein 2002) have been partly addressed. Potential benefits in preventing iodine and/or iron deficiency are much increased subsequent to the ante-natal or post-natal intervention, including more and better education for children, greater productivity throughout life, and a better quality of life. Likewise the impact or effects of micronutrient interventions can be wide-ranging, and consequently not all will be captured and considered e.g. the empowerment of women with vitamin A home gardening programmes (Bushamuka et al. 2005). An example of this is from China where a traditionally high IDD prevalence town had virtually no out-marrying. After salt iodization, not only did the economic prosperity of the town go up but also there was an observed increase in out-marriages (Hetzel & Pandav 1997). Other more distal benefits of programmes extend into improved livestock, crops and other agricultural benefits (Hetzel & Pandav 1997, Bouis 2003, Hetzel 2004, Andersson et al. in press).

Table 6.4: Selected benefit: cost ratios for investments that reduce micronutrient deficiencies (based on Hoddindott 2006).

Deficiency	Intervention modality	Range of benefit: cost ratios	Size of population at risk
Vitamin A deficiencies in pre-school children	Supplements	4-43	128 million children
Iodine deficiencies in women of child-bearing age	Fortification (USI)	15-520	Globally, 2 billion people have iodine deficiencies
Iron deficiencies (general population)	Fortification	176-200	3.5 million people
Iron deficiencies in pregnant women	Fortification and supplementation	6-14	67 million pregnant women, annually

Because the calculations of cost-effectiveness and cost-benefit are a function of methodological differences, exchange rates, time, context, local price differences and the population base, these studies are of limited utility in terms of being able to be fully extrapolated (Levin et al. 1993). However together they do demonstrate a relatively high benefit-cost ratio for micronutrient interventions (Levin et al. 1993, Behrman, Alderman, Hoddindott 2003, Copenhagen Consensus 2003, Mason, Musgrove, Habicht 2003). While more information and analysis are needed, and some of the earlier studies are now somewhat dated, with a great deal of recent activity e.g. the Copenhagen Consensus in 2004, 2006 and 2007 (Copenhagen Consensus website), the current position might be summed up as in Table 6.4. It is clear there is good reason to markedly increase the use of benefit-cost studies for appropriate and strong advocacy for micronutrient interventions.

6.8 Summary conclusions

Overall, given the magnitude of the task, programmes against micronutrient malnutrition should be considered a success, at least partly. At the national level, most countries do not have a food security problem, but problems of household dietary deficit and individual malnutrition are still common among low-income populations, and social inequalities in nutrition and health experience persist (Darnton-Hill & Coyne 1998, World

Bank 2006, UNDP 2006). As noted, micronutrient malnutrition is more often a matter of dietary quality, although undernutrition in general and micronutrient malnutrition almost invariably are part of poverty. Socio-economic improvement has played a large role in the biggest success stories e.g. South East Asia, and fortuitous, but imaginative opportunities, such as adding vitamin A to national polio campaigns.

The implications of positive trends when identified, and that are important for programming, include: how to sustain the trends; how to generate permanent, nationally-owned solutions; how to achieve full coverage using all implementation modalities, with an emphasis on adequate monitoring and quality control. If repeat surveys do not show a positive trend, the constraints, and reasons why not, need to be identified and corrected- this may include how to get further resources and how to sustain any subsequent progress (Mason et al. 2004). Often, this boils down to how to develop and implement effective, large scale programmes suited to conditions and resources of poor countries. This scaling-up of known interventions is proving to be the main push of the 2000s (Lippeveld & Orobaton 2006) e.g. being a main thrust of UNICEF's 2006-2009 Medium Term Strategic Plan. It is a focus of much of the re-invigorated interest of donors for child survival activities, hopefully not forgetting that it needs to be child survival *and* development, mostly based on the evidence base of the 2003 Lancet articles by the Bellagio Child Survival Study Group (e.g. Jones et al. 2003).

There is a good evidence base for intervention efficacy for the main public health public health micronutrient interventions with increasing experience and evidence for national scaled-up interventions.

(i) Efficacy trials have demonstrated from studies, first in Indonesia and then in Ghana, India, Nepal, the Philippines and elsewhere, that high-dose vitamin A supplementation of children results in significant reduction in the prevalence of clinical vitamin A deficiency.

(ii) Efficacy of the addition of iodine by the iodization of salt, and supplementation as appropriate, is established in reducing the prevalence of cretinism, goitre and improving population iodine status and socio-economic development.

(iii) Trials have demonstrated the efficacy of iron tablet supplementation in reducing anaemia prevalence.

(iv) Zinc therapeutic supplementation has been demonstrated in the treatment of diarrhoea and may well have a role in prevention of both diarrhoea and respiratory disease.

(v) Multimicronutrients have been shown to have a small but consistent impact on reducing the number of low birth weight babies, and the average weight; and may have a role in part of the treatment of HIV/AIDS.

Effectiveness is being established for all the micronutrient groups above, but has far too often not been properly monitored and evaluated when programmes have been scaled up. It seems fair to say that vitamin A programmes can be effectively scaled-up as in the effectiveness of coverage in the eleven Asian countries they examined, where Mason et al. (2004b) concluded that vitamin supplementation of children had plausibly contributed to the reduction in clinical vitamin A deficiency and its near elimination in many countries, but the impact may be lower on subclinical vitamin A deficiency. Only a couple of countries, Mali (Schémann et al. 2002) and Nepal (Thapa, Choe, Retherford 2005) have demonstrated a likely association. Similarly fortification programmes, even in poorer economies, can be effective, although again the national level studies, especially for iron fortification, have been inadequately evaluated. Zinc and multimicronutrient interventions are just now being assessed for effectiveness, the latter so far only in emergency situations (de Pee et al. 2007). IDD interventions, particularly USI, have been the most studied and effectiveness is universally accepted (Hetzel et al. 2004), with the constraints and facilitating factors discussed in this chapter. National data on salt iodinization show a consistent reduction in the prevalence of IDD but the evaluation of impact is constrained by lack of biochemical data and the lack of urinary iodine data to programme data- a recent updating of their database by WHO using UI addresses this as far as the available national data allow (WHO 2004). For iron, the consensus concludes that while efficacy is established, the effectiveness has yet to be demonstrated by most country-level data.

Above all, sustainability must be included in any assessment of programme success and has not always been done. Based on the evidence summarized in this chapter, the summary Table 6.5 lists the most common features that should be part of the planning and implementation of any micronutrient programme to ensure effectiveness and sustainability.

Table 6.5: Common features that should be part of the planning and implementation of any micronutrient programme

- Coordination at all levels
- Knowledge of size and implications of problem by decision makers
- Advocacy to ensure knowledge of impact on individuals and families at all levels of society and hence ownership (including inspiring local, or national, charismatic leaders who often seem to be an essential ingredient)
- Established national technical and inter-sectoral committees
- Sustainable financial support
- Special attention to the poorest and most marginalized with parallel implementation of poverty reduction programmes
- Life cycle/course approach
- Facilitating legislation with adequate quality control
- Capacity building and health systems strengthening
- Clear identification and definition of time bound goals/targets at all 4 levels of governance
- The involvement of women in decision making
- Good community infrastructure
- Improved governance at local and national level (including reduction of impacts of social conflict and national disasters where possible)
- Effective social mobilization
- Integration with other services but which may not necessarily apply with all micronutrients or all programmes

One of the consistent factors appears to be that it is essential to have a very broad coalition, with complementary and often overlapping roles. The multi-sectoral, multi-intervention approach has gone through several iterations: initially single micronutrient 'silo' approach, which may well have been appropriate in the initial launching of these interventions, then a very integrated approach; and now a more country-specific approach. The integration now being addressed more directly is through the integrated 'Child Health Week'-type approach that addresses the Child Survival evidence base and the presumed need to not have relatively expensive separate mechanisms for delivering goods and services, as well as the recognized inadequate health systems in many poorer countries and human resource lack of numbers and capacity. However, there is still a way to go, especially in some countries. Also a note of caution has been expressed about this latest iteration in countries already suffering from severe constraints, 'ill-conceived and uncoordinated integration of vertical programmes into a broader health system may end up hampering what little health care is already available'

(Peeling 2006). This would be particularly so where there is dedicated funding to a programme e.g. the CIDA funds for vitamin A.

This is not to say it should not be done but cautiously, adding something like deworming and then expanding beyond the trial areas as successfully done in Nepal, or the number of services such as ITN (bednets) in malarious countries. As seen in earlier chapters it would seem logical that complementary approaches of nutrition education, fortification, dietary diversification and supplementation are most likely to ensure sustainability. The micronutrient goals that have been endorsed by over 160 countries at a variety of fora, have been enormously helpful in getting micronutrients the attention they have received. The time has now come to look at how these need to be redefined but in the opinion of the author, they still have a critical role to play.

The strengthening and expansion of the partnerships should continue, and common, locally agreed-to goals and responsibilities designated that reflect each partner's comparative advantage. There are many examples where this is happening. While much is still unknown about micronutrients, their effects on health, their interactions with one another, how to improve status and so on, there is certainly enough known to be actively pursuing and scaling-up the strategies currently being used. These do however need to be further developed, refined, 'operationalized', tested, adapted to local conditions, evaluated and monitored. An increasing opportunity, somewhat accelerated by human and financial resource constraints is the linking of disease control programmes to other interventions such as micronutrient delivery. This has been described as 'pro-poor' strategy that might have particular applicability to rural Africa (Molyneux & Nantulya 2004). There are good precedents here in micronutrient deficiencies prevention and control as e.g. adding vitamin A to NIDs, and now to such programmes as the 'Accelerated Child Survival and Development' programmes in West Africa, currently being evaluated by the original Bellagio Child Survival Group.

What then is the future for programmes designed to address micronutrient malnutrition: will funding be continued, and will the new goals be reached? The next chapter (Chapter Seven) will look at the goals, and, using the identified facilitating and inhibiting factors, attempt to analyze the likely future and chances of success.

Appendix 6.1

A Conceptual Framework for vitamin A interventions

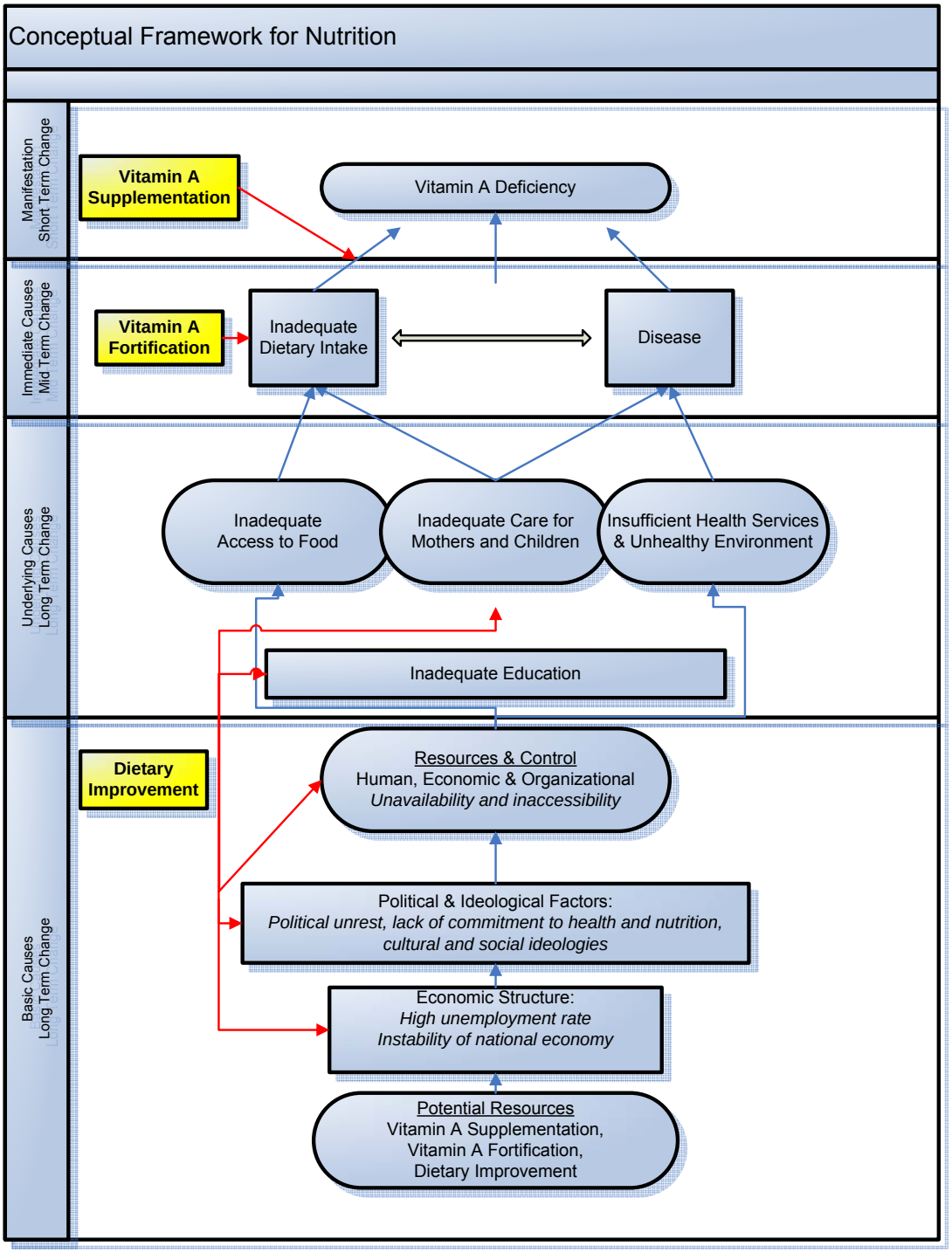
Vitamin A deficiency, like other micronutrient deficiencies, is the result of a complex process of interaction among biological, social, economic, political, and cultural factors, a fact often ignored when looking for sustainable simple and cost-effective interventions. Using the UNICEF conceptual framework for nutrition (Fig.6.1), Pak and Darnton-Hill aimed to develop a conceptual framework for vitamin A deficiency as a way of identifying which are the more, or less, cost-effective interventions (Pak & Darnton-Hill 2006 unpublished paper). The immediate cause of vitamin A deficiency, and the consequent mortality and morbidity, is insufficient intake of vitamin A, often compounded by concurrent diseases such as diarrhea disease, pneumonia, or respiratory disease, which increase bodily utilization and urinary loss of vitamin A (West & Darnton-Hill, 2001). Vitamin A deficiency is due to a range of underlying causes, such as inadequate access to vitamin A rich foods, inadequate care of children and women, insufficient health services, unhealthy environment, and inadequate education. More distal causes of vitamin A deficiency include ineffective and inequitable economic structures, political and ideological factors, and non-availability and inaccessibility of resources.

Each vitamin A intervention- supplementation, fortification, dietary diversification and socio-economic and cultural change, is closely related to the conceptual framework in that it uses various resources to improve economic structure, political commitment and support, as well as availability and accessibility to commodities and resources in order to control vitamin A deficiency, although each approach differs from the others.

Supplementation is, demonstrated earlier in Chapter 5, the most widely implemented intervention due to its cost-effectiveness and capacity to achieve high coverage rate in a short period of time. As seen in the conceptual framework below, vitamin A supplementation programmes do not necessitate inducing sustainable changes in basic, underlying, and immediate causes to vitamin A deficiency. In addition, the designing of vitamin A supplementation programmes is done at macro and global levels; therefore, the policy tends to be top-down oriented. Such an approach ensures immediate increase in vitamin A levels among beneficiaries, and the impacts are relatively easy to be monitored and evaluated. However, implementing vitamin A supplementation programmes do not result in the active involvement of beneficiaries to create and change policies to improve their nutrition status. In addition, sustaining this intervention has been questioned because of its heavy dependence on external funding for the supply of supplements; difficulty in reaching all high-risk populations; narrow targeting of beneficiaries such as children under five years of age and post-partum women; and, most important, inability to affect the root causes of vitamin A deficiency in a sustainable way (Jones et al. 2005).

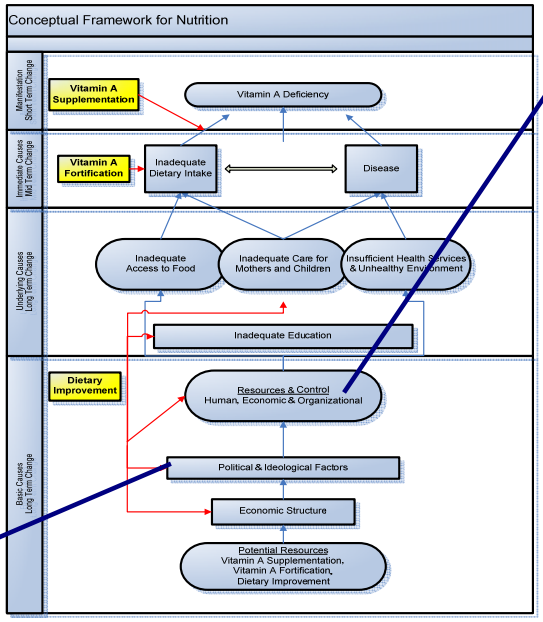
Although vitamin A fortification programmes have often not been as successful in less developed countries due to difficulties with finding suitable fortification strategies, several cases, such as in Central America, with the fortification of sugar, have proven to be effective (Dary & Mora 2002). Vitamin A is being increasingly used as a fortificant in various food sources such as oils and fats such as margarine. One of the most unique characteristics of a vitamin A fortification programme is the role of economic structure as the major determinant factor to its success. Vitamin A supplementation programmes are minimally affected by the economic structure of a country as funding is often external; on the contrary, vitamin A fortification programmes are heavily influenced by national and global economic conditions. For instance, a sudden market decline in sugar became the major cause of halting the sugar fortification programme in the Philippines (Darnton-Hill & Nalubola 2002). Cooperation among central government, industry and donors is needed to sustain vitamin A fortification programmes, which has been the case in Zambia (Fusco & Serlemitsos, 2001), although a large amount of external resources have also been necessary, and programmes are not yet sustainable. As seen in the conceptual framework (below), vitamin A fortification utilizes available resources to increase dietary intakes of vitamin A by intervening at the immediate cause level. However, similar to vitamin A supplementation, fortification programmes do not address the underlying causes of vitamin A deficiency and are top-down policy oriented. Moreover, the positive impacts of food fortification are limited to the people who have access to fortified food, often excluding marginalized populations with little consumer power (Dary & Mora, 2002).

The following pages provide facilitating and constraining factors to successful interventions in a broader perspective.



Source: UNICEF. (1990). Strategy for improved nutrition of children and women in developing countries. Policy Review Paper. E/ICEF/1990/1.6. New York: UNICEF.

Vitamin A Supplementation



Political and Ideological Factors

Facilitating Factors	Constraining Factors
• Enlarged support for VAS in governmental cadres at all levels • Studies conducted by the country on VAS previous to VAS distribution initiatives	• Strong opposition to VAS by leaders of a country • No coherent network of people who understand and believe in benefits of VAS • A perception that sub-clinical VAD is not a problem in a country
• Cost effective policy • Consistent and clear policy	• No policy directives from governments • Operationally infeasible policies • No policy or guidelines to provide supplementation to post-partum women
Government's commitment of its financial resources for VA capsules	Government's inability to take up part of the VAS costs

Organizational Resources

Facilitating Factors	Constraining Factors
• Storing, distributing, manpower infrastructure and reporting system available at every level • Flexibility to move excess supplies from one sub-center to another to meet shortages • Existence of surveys that provide information on coverage rates and other key information for supplementation of children • Nation-widely organized campaigning efforts by using media, which includes newspaper, radio and TV • Identifying at-risk population group by institutionalizing an effective monitoring and reporting system • Incorporating VAS distribution recording and reporting into monthly public health database • Joint micro planning of VAS and immunization	• Data gathered does not trigger action • Irregular and insufficient supply of VAS • Lack of systematic tracking of supply shortages with built-in triggers for corrective action • Weak supervision and monitoring of VAS distribution • Invalidity of survey questions • Unreliability of the data routinely reported • Lack of distribution infrastructure • Geographical characteristics of country that may hinder adequate and timely supply of VAS • Fixed quantity supply for all blocks in the country that ignores vast differences in needs based on population

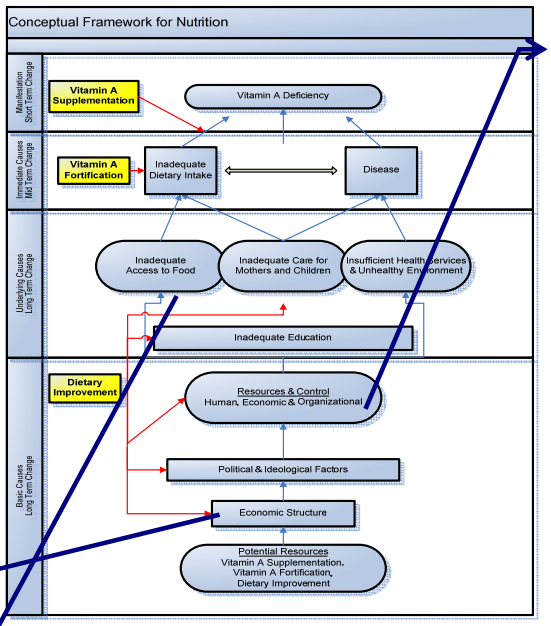
Human Resources

Facilitating Factors	Constraining Factors
• Adequately trained frontline and village-level workers • Competent and motivated staff • Policy-makers' awareness of the benefits of VAS • Existence of comprehensive training program for health workers who are part of the VAS program	• Workers and providers do not know the consequences of VAD or the correct dosages to be provided to specific age groups • High workload for community health workers • Insufficient number of staffs • Caretakers' unawareness about benefits of VAS for their children

Economic Resources

Facilitating Factors	Constraining Factors
• Consistent donor support • Government's budgetary resources to buy VA capsules	• Heavy dependence on donation • Government's inability to take up the cost for VAS

Vitamin A Fortification



Economic Structure

Facilitating Factors	Constraining Factors
• Effective partnership between government and industry by reconciling public nutrition and industry's profit maximizing interest • Facilitating acceptance of food fortification in a global market so that neighboring countries may agree on the same technical standards of food fortification	• High production cost due to high price of fortificant and capital costs • Total cost increase of fortified products which may result in decrease of profits of producers unless they can transfer the cost to consumers • Open trade market that allows importing and selling non-fortified products at a lower price • Socio-economic constraints of the people in need of vitamin A

Political and Ideological Factors

Facilitating Factors	Constraining Factors
• Government's political commitment expressed by making fortification an official program	• Unawareness of policy makers about the cost-effectiveness and benefits of vitamin A fortification • Strong objects against fortified products by national leaders and/or consumers • Ineffective law enforcement in quality control

Organizational Resources

Facilitating Factors	Constraining Factors
• Collaboration among governments, food companies, scientific establishments and development agencies • Open communication between private and public sectors • Clear delineation of responsibility and accountability for the industry and government in assuring and controlling quality of fortified products • Adequate regulations by both governments and international bodies on public-private partnerships • Monitoring system in place to assure quality and an adequate level of vitamin A in fortified products	• Food fortification policies centered on the interest of private market, rather than public-interest • Weak industry motivation and government political commitment • Unavailability of reliable market research on acceptability of a fortified food by consumers • Unavailability of studies on food consumption pattern and how fortification affects properties of foods • Inadequate and ineffective distribution system

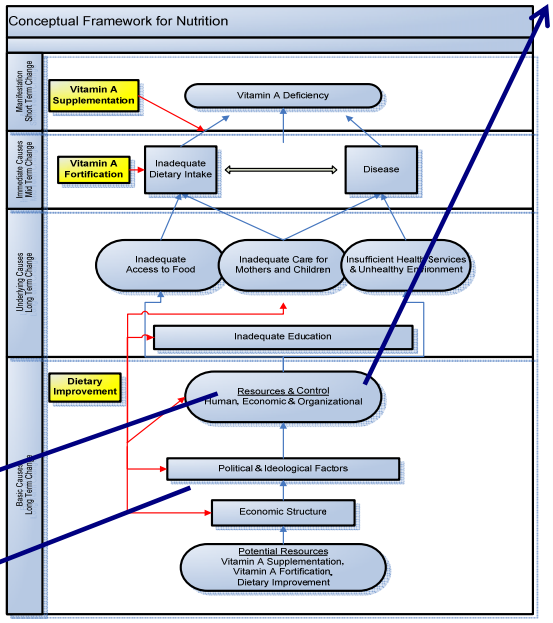
Human Resources

Facilitating Factors	Constraining Factors
• Policy makers who see the benefits and effectiveness of vitamin A fortification • Availability of nutrition education in order to change increase people's awareness of consuming fortified products • Availability of training in fortification technology and monitoring	• Lack of access to fortified foods due to geographical, social and cultural reasons

Economic Resources

Facilitating Factors	Constraining Factors
• Private philanthropic support for nutrition e.g. support form Bill and Melinda Gates Foundation • Collaboration between private and public sectors to lower the prices • Minimal or no cost increase to the consumers, resulting from producing fortified products	• Low consumer purchasing power seen among the poor • High production costs

Dietary Improvement



Political and Ideological Factors

Facilitating Factors	Constraining Factors
• Government's basic political support, e.g. through appropriate research and extension services, provision of basic access to land and water and supportive land use regulations • Participation of both private and non-governmental organizations and governmental ministries • Considering diet improvement strategy in the context of a broader national food security strategy	• Lack of political commitment to support dietary improvement programs, e.g. due to prioritization of supplementation and/or fortification • Lack of collaboration between national governments and local governments • Instable government structure • Actions taken without thorough situational assessment and analysis • Social customs that prevents many from eating vitamin A-rich food, e.g. such as low status of dark-green leafy vegetables as food in Nepal

Organizational Resources

Facilitating Factors	Constraining Factors
• Building on traditional knowledge and methods of home gardening in the region in order to prevent resource constraint problems • Effective communication strategy to circulate knowledge and skills among extension workers, group leaders, gardeners and their families • Integration of nutrition awareness education into trainings for home gardening, home-processing and plant breeding techniques • Nutrition education on breast-feeding, weaning foods, maternal diet during pregnancy and lactation, and food preparation and hygiene • Community ownership of the project, e.g. projects designed and monitored by the community members • Using both modern and traditional mass media to educate people about dietary improvement projects • Education and communication to change knowledge, attitudes, and household dietary practices	• Poor design of projects, management strategies and planting materials inappropriate for the local condition • Lack of thorough situational assessment and analysis before implementing a project • Incorrect identification of major food crops and inadequate assessment of their importance in the diet based on people's knowledge on food and nutrition

Human Resources

Facilitating Factors	Constraining Factors
• Involvement of the whole family • Understanding roles of women and children in home-gardening projects • Trained local women volunteers • Motivated and charismatic group leaders • Examining how benefits are distributed among men and women	• Division of labor by gender which creates and exacerbates time and labor constraints to women

Economic Resources

Facilitating Factors	Constraining Factors
• Gardening that is possible with virtually no economic resources by using locally available planting materials and other resources (No or little barrier to entry) • Home gardening being used as sources of vitamin A intake and supplementary income	• Home gardening being unreliable as a steady income for poor households • Lack of international donor's commitment to providing financial support to NGOs to support start-up costs and technical supports

Environmental Resources

Facilitating Factors	Constraining Factors
• Various techniques developed for overcoming environmental constraints	• Low soil fertility • Restricted access to water • Poor diversity of food crop production • Poor access to fertile farmland and fishing

Economic Structure

Facilitating Factors	Constraining Factors
• Effective safety-net that protects people during economic hardships • Collaboration between public and private sectors to reduce and stabilize price of vitamin A rich products • Effective and competitive market that provides vitamin A rich products at affordable prices • Low labor and input prices for home gardening	• Instable national economy • Low employment rate • Low GNP and GDP

The conceptual framework used here has four purposes. Firstly, the framework is used to differentiate between factors causing vitamin A deficiency and determinant factors to successful vitamin A interventions. Secondly, the initial chart is used to recognize the different socio-governance levels at which each programme is primarily implemented. As seen in the chart, vitamin A supplementation directly intervenes at the outcome (manifestation) level by supplying supplements; the fortification programme is implemented at the immediate cause level by supplying vitamin A fortified foods; and the dietary improvement programme is implemented at the basic cause level. Thirdly, the framework is used to examine how all three intervention approaches, although implemented at different levels, focus on changing and utilizing factors at the basic cause level. For instance, even though dietary improvement is the only strategy implemented at the basic cause level, all three interventions utilize and create factors at the basic cause level in order to enhance the strategies, making them more effective at reaching a large population. Fourthly, the chart is used to show that only dietary improvement strategy utilizes chain effects. For example, although a vitamin A supplementation programme procures and utilizes a large number of economic resources to create logistics for more effective distribution of vitamin A supplements, such an effort does not address the lack of economic resources that causes vitamin A deficiency initially, nor does it alter the underlying causes of vitamin A deficiency.

Examining facilitating and constraining factors to successful supplementation and fortification programs reveals that these programmes are heavily dependent on donations and top-down-policy oriented. As noted earlier this is also true of immunization programmes and increasingly the Global Fund activities in HIV/AIDS, Tuberculosis and Malaria (Ooms, Derderian, Melody 2006), but remains a concern. In addition, the focus of resource utilization is on increasing the effectiveness of a supplement distribution system or promoting compliance among consumers to buy fortified foods; therefore, sustainability of the interventions and eliminating vitamin A deficiency largely depends on external capacity to continuously provide donation and legal enforcement. On the other hand, dietary improvement utilizes resources to address core causes of vitamin A deficiency, but is less quickly effective and relies on socio-economic change, inmost cases. A focus on dietary improvement has greatest potential to empower consumers to make well-informed daily choices to improve their and their children's nutrition status, increase their consumer power by actively engaging in market system and their involvement in designing programs that can best serve their needs (Bushamuka et al. 2005) but is less effective in the short term and relies considerably on broader externalities such as economic development and decreasing internal inequities.

Chapter Seven

7.1 The next decade- background

The optimism at the beginning of the first 'micronutrient decade' (1990-1999) was largely vindicated by impressive progress in addressing deficiencies of vitamin A and iodine, although little progress was made in iron deficiency prevalence. Reflecting an understanding at the start of the new millennium in 2000, that many social, health and nutrition indicators had not much improved, and that global security and environments were deteriorating, the next decade (2000-2009) was entered more warily in terms of achievable goals. There were some signs of hope for global change- the Millennium Declaration and the near global consensus on the Millennium Development Goals (MDGs) (UN 2000, 2001b). But even here, despite the promises of the richest nations at Monterey (UN 2002a), it was clear that, again, promises for funding support are far exceeding the actual contributions (UNDP 2003, UNDP 2005). Nevertheless, the UN Special Session on Children, itself a promising landmark, developed new goals in 2002 (UN 2002a). This chapter looks at that next decade (2000-2009) and after, to the subsequent five years to 2015, and identifies remaining issues, reviews progress and suggests some future directions through a 'micronutrient lens'.

7.2 New goals

Five years ago two major UN meetings impacted directly on the global goals for micronutrients. The first was a UN Special Session on Children, effectively a decade later follow-up to the World Summit for Children of 1990, when the first micronutrient goals were established (UNICEF 1990, UN 2002b). While these were not reached, as was seen in the Chapter 5, considerable progress was made; enough that it was generally felt to be worthwhile to establish another series of goals. These were again overly optimistic, but many, probably most, argue that the concept continues to provide useful international impetus. For various reasons, not least the September 11, 2001, destruction of the twin World Trade Center towers in New York, this session was not held until May 2002. At this session a new set of goals, essentially the business plan for UNICEF over the next 10 years, were proposed and endorsed. Although different in

essence from the earlier, first set of goals they also included a combined goal for micronutrients (UN 2002c):

"Achieve sustainable elimination of iodine deficiency disorders by 2005 and vitamin A deficiency by 2010; reduce by one third the prevalence of anaemia, including iron deficiency, by 2010; and accelerate progress towards reduction of other micronutrient deficiencies, through dietary diversification, food fortification and supplementation".

7.2.1 The UNGASS (2002) Goals

These goals were designated by the UN Special Session, and are known within UNICEF as the 'World Fit for Children' (WFFC) goals and were more heavily slanted to protection of the child this second time, and there was even uncertainty at one point if there was to be a micronutrient goal. Then the first draft had a goal that did not mention iron. This was hotly debated. Many respected nutritionists argued, oddly in the opinion of the writer, that because no progress had been made in the first decade goals, there was no point having another iron deficiency goal in the WFFC goals. This focus on the lack of progress on prevalence levels however, under-estimated the operational research that had been going on, clarifying such issues as the efficacy of weekly dosage versus daily, compliance, and increasing experience with, and research on, fortification and multimicronutrients. There was a strong push for increased attention to fortification, and for supplementation from a somewhat different lobby, and again much operational experience had been gained. As has been so often the case, dietary based measures lacked a strong enough advocate (donors tending to favour supplementation), whereas some international NGOs and donors such as Canada and the US were encouraging a strong push for public-private sector activities, which fortification quintessentially is. The final goal that emerged was as above.

Structurally UNICEF has used a framework whereby their four-year Medium Strategic Plan (MTSP) (2006-2009) is seen as the Agency's work plan; the World Fit for Children goals (2000-2010) as the business plan, and the Millennium Development Goals (see below) as the framework towards which all Agencies and Governments are heading (2000-2015). There was an implied intention that simple indicators would be used that allowed countries and international agencies to decide when this goal has been reached

(UNICEF 2002). The whole concept of global goals has since been debated (e.g. ACC/SCN 2001) and will be discussed later in this chapter.

7.2.2 The Millennium Declaration and the Millennium Development Goals

Two years earlier in 2000 another UN Special Session had established the Millennium Declaration and Goals (UN 2000). This had then been followed nearly two years later by the publication of the Monterrey Consensus at which the richest nations on earth committed themselves to funding the achievement of these goals (UN 2002a). The Millennium Declaration and the accompanying Millennium Development Goals (MDGs) were, and are, an ambitious attempt to expand goals in scope while keeping the number small (at eight) (Table 7.1). Inevitably this has meant a broader stroke. They aim to reduce poverty and improve the lives of all peoples and were agreed to at the largest gathering of world leaders ever at the Millennium Summit in September 2000 (UN 2000). The stated aim is: 'The Millennium Development Goals (MDGs) aim to reduce the striking inequalities between the rich and poor countries, and between the rich and poor populations within countries (UN 2000). For each goal one or more targets have been set, most for 2015, using 1990 as a benchmark (UN 2001, 2002c).

These eight goals (Table 7.1) did not specifically address micronutrients, and only tangentially nutrition, although goal number 1 did call for the eradication of extreme poverty and hunger. Since then, there has, however, been considerable effort and creativity demonstrating how virtually none of the Millennium Development Goals (MDGs) will be achieved without 'mainstreaming nutrition', including micronutrients (SCN 2004, Veneman 2004). In a way that most did not predict, and which some UN Agencies, perhaps especially UNICEF were in fact accused of resisting, the commitment to these goals has become now almost universally accepted by all Member States, International Agencies and Non-Governmental Organizations (NGOs), and is an integral part of the UN harmonization process. The challenge has therefore been to demonstrate the essential nature of micronutrient interventions to achieve these.

While all the goals indirectly or directly (MDG1) address poverty reduction, many goals quite directly address results that would lead to improved health: eradication of extreme poverty and hunger, achievement of universal primary education, promotion of gender

Table 7.1: The global challenge: The Millennium Development Goals and some of the more relevant targets* (UN 2002b).

Goal	Target
1. Eradicate extreme poverty and hunger	Halve, between 1990 and 2015, the proportion of people whose income is less than one dollar a day; and those who suffer from hunger
2. Achieve universal primary education	Target for 2015: Ensure that all boys and girls complete primary school
3. Promote gender equality and empower women	Targets for 2005 and 2015: Eliminate gender disparities in primary and secondary education preferably by 2005, and at all levels of education by 2015
4. Reduce child mortality	Target for 2015: Reduce by two thirds the under-five mortality rate
5. Improve maternal health	Reduce by three-quarters, between 1990 and 2015, maternal mortality ratio
6. Combat HIV/AIDS, malaria and other diseases	By 2015 to have halted and begun to reverse the spread of HIV/AIDS and the incidence of malaria and other major diseases
7. Ensure environmental sustainability	Targets: • Integrate the principles of sustainable development into country policies and programmes and reverse the loss of environmental resources • By 2015, reduce by half the proportion of people without access to safe drinking water • By 2020 achieve significant improvement in the lives of at least 100 million slum dwellers
8. Develop a global partnership for development	Targets: • Develop further an open trading and financial system that includes a commitment to good governance, development and poverty reduction - nationally and internationally • Address the least developed countries' special needs • Deal comprehensively with developing countries' debt problems • provide access to affordable essential drugs in developing countries • cooperate with the private sector to make available the benefits of new technologies - especially information and communications technologies

*in many cases the targets are paraphrased to be shorter

equality and empowerment of women, reduction of child mortality, improvement of maternal health, combating HIV/AIDS, malaria and other diseases, ensuring environmental sustainability and strengthening and developing of a global partnership for development (UN 2001) (Table 7.1). From an UN perspective, and perhaps especially UNICEF's, six of the eight MDGs will only be met when the rights of children to health, education, protection and equity are fully protected.

An important factor in current approaches to goals, especially the MDGs has been the publication identifying the magnitude of avoidable child deaths in low income countries and of ways to improve child survival (Black, Morris, Bryce 2003, Bryce et al. 2003), Neonatal survival (Lawn et al. 2005, Martines et al. 2005), and the likely costs of doing these (Bryce et al. 2005, Evans et al. 2005a, b). The economist Jeffrey Sachs has taken a slightly different approach, as adviser to the UN Secretary-General, in the Millennium Villages model (Sachs 2001, UN Millennium Project 2005); the cost of how much might be needed and that he calculated is an estimated figure somewhat similar to those of Bryce et al. (2005) and others. A series of articles have since come out, estimating the costs, and also cost-effectiveness of many of the proposed child survival interventions (Tan-Torres Edejer et al. 2005, Bryce et al. 2005). However, it has also been noted that one must also move beyond just cost-effectiveness; money, infrastructure and information are also vital (Wibulpolprasert, Tangcharoensathien, Kanchanachitra 2005), as are considerations of equity (Victora et al. 2003, Chopra & Sanders 2004, Evans et al. 2005b). So far, despite repeated promises, the wealthier countries are not coming up with such funds (UNDP 2003, UNDP 2005).

These articles have ensured widespread recognition that due to poverty and lack of access to basic social services, more than 10 million children under five years of age, nearly half of them in their neonatal period, are dying every year of preventable diseases and undernutrition (Black, Morris, Bryce 2003, Bryce et al. 2003). Complications related to pregnancy and childbirth and maternal anaemia and malnutrition are likewise killing more than half a million women and adolescents each year, and are injuring and disabling many more. More than one billion people cannot obtain safe drinking water; 150 million children under five years of age are malnourished; and more than two billion people lack access to adequate sanitation (UN Millennium Project 2005). Over half of these deaths have undernutrition, including of micronutrients, as the underlying factor (Rice et al. 2000, Black, Morris, Bryce 2003, Caulfield et al. 2004). A subsequent series addressed neonatal survival (Lawn et al. 2005, Martines et al. 2005), maternal survival (still in preparation) and others will address infant and child development (Jolly 2007, Engle et al 2007), and also nutrition (in press January 2008).

There has been increased attention to the concept of the ‘poverty trap’ (e.g. UN Millennium Development Project 2005), earlier espoused by King and others (King &

Elliott 1990), but which fell from favour with the rise of economic rationalism as the prescription for economic development (World Bank 1993, World Bank 2001). With the World Bank's increasing presence in development (World Bank 2001), and more recently a re-alignment on their approach to nutrition (World Bank 2006a), and belatedly the recognition that globalization has not generally been good for the very poor (Chopra & Sanders 2004, UN Millennium Development Project 2005, World Bank 2006b), there has also been a tentative recognition by the World Bank and others that more distal and geo-political factors must be considered if health is really to improve in the developing world (Chopra & Sanders 2004, Darnton-Hill et al. 2005a, Darnton-Hill, Bloem, Chopra 2006). Although being strongly resisted by the affluent countries, there is an acceptance (including by these same nations in other fora), that current global trade is a source of gross inequity and a hindrance to sustainable development. The Australian Trade Minister Mark Vaile has been quoted in the New York Times, as pointing out 'that a typical cow in the European Union receives a government subsidy of $2:20 a day- more than what 1.2 billion of the world's poorest people live on every day' (New York Times 2005). Consequently there is now a renewed push to break the intergenerational cycle of malnutrition and poor health by providing a safe and healthy start in life for all children; providing access to effective, equitable, sustained and sustainable primary health care systems in all communities, ensuring access to information and referral services; providing adequate water and sanitation services; and promoting a healthy lifestyle among children and adolescents. The role of micronutrient interventions will be of relatively less importance overall- but critical.

It seems there is also greater acceptance now that for effectiveness and sustainability to achieve these goals and targets, the best interests of the child, consistent with national laws, religious and ethical values and cultural backgrounds of its people, and in conformity with all human rights and fundamental freedoms, need to be taken into account. A recent paper has suggested that care must be taken that society-wide improvements, in this case in under five mortality, must be spread to the most disadvantaged, as improvements seem as likely to increase inequalities as to decrease them (Moser, Leon, Gwatkin 2005) at least in less poor quintiles. Although the wealthiest nations are not yet living up to their promises, there has been some encouraging moves recently (less so from the USA) e.g. at the Gleneagles G8 meeting, when considerably more commitments were made, especially for Sub-Saharan Africa,

including debt forgiveness for some 19 of the Least Developed Countries (LDCs) (Financial Times 2005) but much more is needed (Chopra 2004).

Although it will be argued here that many of the goals will not be achieved without addressing micronutrient deficiencies, especially MDGs 1, 4 and 5, micronutrients, as noted earlier, are not specifically mentioned anywhere, nor is the emerging global epidemic of obesity and other noncommunicable diseases (WHO/FAO 2003, Darnton-Hill & Chopra 2006). It seems likely that there will not be global goals for micronutrients in another future UN Special Session, although they will no doubt continue to be addressed in workplans and strategies to reach MDGs e.g. vitamin A supplementation in Child Survival programmes such as the Partnership for Maternal, Neonatal & Child Health (PMNCH 2005, Dalmiya, Palmer, Darnton-Hill 2006). This approach, for example for the Accelerated Child Survival and Development (ACDS) being largely successfully applied by UNICEF in West Africa, tends to commodify micronutrients such as vitamin A and zinc as a child survival implementation tool such as immunization and bednets, bringing into question sustainability, as well as the availability of funding for strategies involving behaviour change, and food-based approaches, despite evidence of their effectiveness (Torlesse, Kiess, Bloem 2003, Quinn et al. 2005).

7.3 Analysis

Current programmes and remaining issues

The analysis looks at the likelihood of the World Fit for Children (WFFC) goals for micronutrients being reached, largely based on the predicted trends from Chapter 5. There will also be some discussion on the likelihood of the best practices discussed in the preceding chapter being adequate for the job, and the likelihood of them being utilized on a large enough scale to make a difference- and particularly to achieve the WFFC goals. It is noted for example that the IDD goal was to be completed by the end of 2005, and while the findings from the MICS surveys and DHSS being done this year (2006) should give a better picture, this goal was not achieved. The Millennium Development Goals for hunger and undernutrition (MDG1, Target 2) and child survival (MDG4) are both unlikely to be reached in many countries at the current rate (UNICEF 2004, UNICEF 2006, Lawn et al. 2007). In acknowledgement of the first, the Executive Boards of UNICEF and WFP have recently approved a global effort for an 'Ending Child

Hunger and Undernutrition Initiative', recognizing that what progress there has been in reducing underweight globally has been very unequal, with some countries, particularly in Sub-Saharan Africa, actually getting worse.

Clearly, because worldwide at least 15% of the global burden of disease can be attributed to the joint effects of childhood and maternal underweight and micronutrient deficiencies (iron, vitamin A, and zinc deficiencies), progress needs to accelerate (UNICEF 2006a). The contribution of undernutrition to the global burden of disease in 2000 has barely changed since 1990. In Africa undernutrition (underweight, iron deficiency, vitamin A deficiency, and zinc deficiency) explains up to 30% of childhood and maternal deaths (Ezzati et al. 2002).

Because of the essential consensus around the need to reach the MDGs, (beyond discussions and disputes on how exactly this might best be done; the suitability of some goals; and, the appropriateness of some indicators in particular), this chapter will now consider micronutrients through the MDGs by identifying the micronutrient contribution that will need to be achieved to reach a particular goal. Several, perhaps all, of the micronutrients will be critical in the achievement of most of the MDGs, in which case this will be addressed with each goal but in detail in the one considered most relevant e.g. iron and MDG5 to improve maternal health, while at the same time being aware that iron deficiency is a factor in MDG2- achieving universal primary education and MDG4, to reduce child mortality (Table 7.2).

The UN Millennium Project and the plan to achieve the MDGs have been criticized on several grounds. Firstly that they do not at present fully recognize the fundamental importance and critical role of good nutrition for a nation's development, and in relation to nutrition, the emphasis is probably too heavily weighted to agricultural relevance. The MDGs have also been criticized as reflecting the priorities of donors and as being unachievable. On the other hand, they have also focussed the attention of the rich world on the health and nutrition needs of the poor countries (Godlee 2005, World Bank 2006b). International goals in general have been criticized as ignoring inter-country and regional differences, being non-sustainable, simplistic and likely to undermine the development of integrated sustainable programme approaches (Arthur 2001).

Table 7.2: Micronutrients and the Millennium Development Goals: framework for examining implications (focus micronutrient in bold).

Goal	Target
1. Eradicate extreme poverty and hunger	Improved diets: vitamin A and ***zinc*** as surrogates for improved quality of diets and iron and zinc as growth-limiting micronutrients
2. Achieve universal primary education	Intellectual potential: ***iodine*** and iron
3. Promote gender equality and empower women	Iron and vitamin A (home-gardening)
4. Reduce child mortality	Known factors in reducing mortality: ***vitamin A*** and zinc
5. Improve maternal health	Role of **iron** and other nutritional causes of anaemia such as folate deficiency
6. Combat HIV/AIDS, malaria and other diseases	Role of ***multimicronutrients*** supplementation and diet and prevention and control of malaria in non-nutritional anaemias
7. Ensure environmental sustainability	Less direct impact although home gardens are an example
8. Develop a global partnership for development	Multisectoral approaches and partnerships essential (chapters 3 & 4)

There is, however, an increasingly acknowledged need to increase the recognition that improved nutrition at critical periods in the life cycle, especially during pregnancy and early childhood, are essential if most of the MDGs are to be achieved (Veneman 2005, World Bank 2006a). This is a challenge when the targets do not address this, or even often the indicators. The Report of the Secretary General "In larger freedom: towards development, security and human rights for all" does not distinguish the child undernutrition target for MDG 1 from the income target, and does not mention malnutrition as being a hindrance for achieving the MDGs, but merely refers to food insecurity and hunger. Poverty reduction and increased food production alone will not solve the nutrition problems facing the poor populations in developing countries. There is also concern that some progress towards the goals, as an average, may in fact leave the least poor behind (Moser, Leon, Gwatkin 2005). Others argue that they are in fact not new, and that early talk of failure is self-defeating (Harcourt 2005), and others see an important role for civil society to keep the process on target (Shetty 2005).

Nevertheless, the MDGs are the framework in which the international community is currently working, especially the UN. Consequently the above framework is used to discuss: undernutrition and zinc (MDG1); iodine (MDG2); vitamin A (MDG4); iron (MDG5); and multimicronutrients (MDG6). While somewhat artificial and with obvious overlaps, it is way of identifying the relationships between policy and programming.

The MDGs are to be achieved by 2015 and there are already dire, but probably realistic, predictions of the failure of many of the goals to be reached, especially in sub-Saharan Africa (UNICEF 2004, 2005, UN 2006, UNDP 2003, 2005, WHO 2005a, b, Dyer 2005). The time-frame of the UN 'World Fit for Children (WFFC) goals is within this current decade (2000-2009) and may well be a surrogate, or at least an indicator, of the likely achievement of the MDGs. Clearly, many other factors are involved as discussed in Chapter 6 (Figure 6.1) - global, distal and proximal factors (UNICEF 1990). The last includes adequate diet, health and family care and adequate health systems and the global or basic causes can include factors such as unfair trade, insufficient aid and the crushing burden of debt (UNDP 2003, Darnton-Hill & Chopra 2006). All these are critical but this chapter focuses on the roles of micronutrients within this framework of broader pre-requisites for health, development and child survival.

7.4 Micronutrients in the progress towards achieving the MDGs

This section takes the eight Millennium Development Goals, identifies the micronutrient contribution needed and assesses the likelihood of the particular micronutrient goal identified in the World Fit for Children (WFFC) Goals (UN 2002c, UNICEF 2002) being reached and the relevant MDG. Although by definition vitamins and trace elements are essential for survival, some are clearly more relevant to public health practice than others. The framework for examining them here can be seen in Table 7.2 and expanded in the Appendix in Table 7.3. Each of the micronutrients will be briefly described in its contribution to one or more goals and then the implications of this: in terms of the Millennium Development Goal being reached; in terms of global health and economic development; constraints to prevention and control; likelihood of the WFFC goal being reached; and finally, future policy and programme implications.

7.4.1 Goal 1: Eradicate extreme poverty and hunger

There are two targets for this MDG. Firstly to halve between 1990 and 2015, the proportion of people whose income is less than one dollar a day; and secondly a non-income measure, to halve the proportion of people who suffer from hunger (UN 2001). The latter has so far received far less attention and is progressing less well (UN 2006, UNICEF 2006). It uses as one of its indicators, the prevalence of underweight children under five years of age (the other indicator is the proportion of the population below minimum level of dietary energy consumption) (UN 2001, Rivera et al. 2006). The diets of the poor tend to be more often characterized by the quality of the diet, even more than the quantity (Calloway 1995). It is often pointed out that in terms of dietary energy, there is enough food globally (FAO 2005), although at an environmental cost that is rarely figured in realistically (Brown 2005). Some micronutrients are themselves growth-limiting and will restrict growth even when there are adequate amounts of energy and protein in the diet e.g. zinc (Golden 1991, Rao et al. 2001, Rivera et al. 2003). Vitamin A, iron and zinc might all be used as surrogates for an adequate diet in that they are more often found in animal foods in prosperous and higher quality diets while diets poor in bio-available iron and vitamin A and zinc, and high in phytates are more typical of diets in poor communities (Allen 1991, Calloway 1995, Bloem, de Pee, Darnton-Hill 2004, Hotz & Brown 2004, Neumann et al. 2007).

Zinc deficiency has long been known to be an important factor in growth and is increasingly recognized as also important in the control of diarrhoeal disease, and probable prevention in diarrhoea and respiratory disease and in reducing overall child mortality (Black 2003). Its prevalence is measured globally according to likely dietary intake due to the difficulty in measuring serum zinc in a way that reflects individual stores. The current estimate is that zinc intakes are commonly inadequate, in half or more of the population in those developing countries with the highest mortality rates (Hotz & Brown 2004) and although there are methodological challenges to estimating it due to unclear prevalence and impact of interventions, has a large effect on the global burden of disease (Caulfield & Black 2004). In the comparative quantification of health risks study done for WHO, Caulfield and Black (2004) estimated the global prevalence at 31% (range=4-73% across regions) and the associated loss of disability-adjusted years (DALYs) attributable to zinc at more than 28 million.

A study in India also showed positive correlations between vegetable and fruit intakes and milk products and with beta-carotene, thiamin and riboflavin intakes and negatively with cereal and legume consumption, and poor environment, family size and iron and phytate intakes (Agte, Chiplonkar, Tarwadi 2005) but zinc is most commonly found in more expensive animal foods which are not accessible to poorer populations. Zinc deficiency therefore places many children in low-income countries at risk of illness and death from infectious diseases. There is now enough solid evidence that zinc supplementation reduces child mortality due to diarrhoea, by lowering the severity of acute diarrhoea, reducing the length of persistent diarrhoea and lowering the chance of another attack (for a couple of months), pneumonia and malaria (Black 2003, Hotz & Brown 2004) that there is now a recommended treatment for diarrhoea with zinc supplementation and ORS, by WHO/UNICEF (WHO/UNICEF 2004, Shrimpton et al. 2005).

Iron deficiency is likely to be even more common: anaemia, due largely to iron deficiency affects one third to one half of the preschool children and women of reproductive age in lower income countries (WHO 2001). Iron deficiency itself affects an estimated two billion people and causes almost a million deaths a year, as well as impairing the mental development of about half of the developing world's children, which also has implications for the second MDG (under which it will be discussed). Because absorbable forms of iron and zinc are found in many of the same foods, and ones infrequently found in poor diets, these high rates of iron deficiency are suggested to be similar in similar populations (Hotz & Brown 2004). Vitamin A deficiency has not been shown to be a growth-limiting vitamin- at least in humans (West & Darnton-Hill 2001).

Although there is better progress on the first target of MDG1 (the ‘poverty target’), again the progress is very uneven across countries (World Bank 2006). There is now increasingly good evidence that alleviating micronutrient deficiencies, especially iron, but also others that are growth limiting, will have quite dramatic effects on economic development. It is an area of potential advocacy upon which the international nutrition and development community have so far failed to capitalize. The effort to acquire these data and evidence has had a long history, and it is often noted animal nutritionists knew this almost as soon as vitamins and minerals were identified (and farmers more from intuition and experience millennia before). Levin et al. in 1993 in identifying disease control in developing countries priorities, made one of the first attempts at quantifying

costs and benefits of micronutrient interventions. McGuire and Galloway built on this a year later to publish the World Bank book on 'Enriching lives' that laid out an economic reason for investing in micronutrient deficiencies prevention and control programmes (McGuire & Galloway 1994). The Micronutrient Initiative then asked an economist and public health specialist together to calculate the cost of iron deficiency (Ross & Horton 1998). Since then they have been joined by more economists (Mason, Musgrove, Habicht 2003, Fogel 2004, Behrman, Alderman, Hoddinott 2004, Alderman & Horton 2007, Stein & Qaim 2007). A particular boost to this line of thinking came from the Copenhagen Consensus when a group of economists were asked what would be the 'best' way to spend an additional $50million on development and micronutrients, particularly interventions to reduce iron deficiency, came up the second recommended choice (Copenhagen Consensus 2004).

Implications

MDG1: More than a billion people still live on less than US$1 a day: sub-Saharan Africa, Latin America and the Caribbean, and parts of Europe and Central Asia are falling short of the poverty target. Approximately 146 million under age five infants and children in the developing world are underweight including almost half the children in South Asia, approximately a quarter of all children globally are at risk of premature death and inadequate development due to being underweight (UNICEF 2006). In Sub-Saharan Africa, the number of underweight children increased from 29 million to 37 million between 1990 and 2003, with little change in the proportion (WHO 2005). At current rates, of the 94 countries (out of 156) for which there are trend data, there is no progress in 21 countries, or it is insufficient in 27, i.e. only half of all developing countries are on track to reach the undernutrition target of MDG1 (UNICEF 2006). Of those not on track, 21 are in sub-Saharan Africa. Nearly three quarters of undernourished children live in just 10 countries, and more than half live in Asia. The MDG is therefore unlikely to be met for many of the poorer countries of the world (UNICEF 2006).

Undernutrition is the single leading global cause of health loss worldwide, and about 15% of the global burden of disease can be attributed to the joint effects of childhood and maternal underweight and/or micronutrient deficiencies (iron, vitamin A, and zinc deficiencies) (Ezzati et al. 2002, 2003). Where prevalence of 'hunger' and undernutrition is high, mortality rates for infants and children under five are also high,

and life expectancy is low. In the worst affected countries, a newborn child can look forward to an average of barely 38 years of healthy life (compared to over 70 years of life in "full health" in 24 wealthy nations). One in seven children born in the countries where 'hunger' (as defined by FAO) is most common will die before reaching the age of five (FAO 2005). Using apparent dietary intakes from food balance sheets, FAO has estimated that there are over 850 million people worldwide undernourished or 'hungry', with a disproportionate number in South Asia (22%) and Sub-Saharan Africa (33%) (FAO 2005). The same report notes that even in the absence of chronic or transitory hunger, populations can still suffer from a lack of essential micronutrients (FAO 2005). Infants and children, and women, at risk of being underweight are more likely to have poor quality diets (Calloway 1995) and in fact, even more suffer from micronutrient deficiencies than from being underweight or lacking food.

Because measures of food deprivation, nutrition and poverty are strongly correlated, countries with a high prevalence of stunted and underweight children also have a high percentage of the population living in conditions of extreme poverty. While poverty is undoubtedly a cause of undernutrition, both hunger and undernutrition can also be causes of poverty. Hunger often deprives impoverished people of the one valuable resource they can call their own: the strength and skill to work productively. Numerous studies have confirmed that hunger seriously impairs the ability of the poor to develop their skills and reduces the productivity of their labour (FAO 2005, World Bank 2006). Consequently the two targets representing both income and non-income outcomes, are inextricably intertwined.

Poverty reduction (MDG 1) is hampered by reduced physical and mental capacity of adults, largely caused by poor growth and nutrition in childhood that cannot be easily reversed. Reduced cognitive ability associated with stunting and lack of proper infant feeding, measurable in lower scores on IQ tests, leads to reduced productivity and earnings across the course of life (Grantham-McGregor et al. 2007). Switching one low birth weight infant to non-low birth weight status yields almost US$1000 in benefits over a lifetime. With about 20 million low birth weight children born every year in developing countries, the costs of doing nothing adds up to around US$20 billion a year among those that survive. Anaemic adults are also less productive with estimated losses of up to 2% of GDP in the worst affected countries. It has been repeatedly demonstrated that

undernutrition contributes to over half of all child deaths (Pelletier & Frongillo 2003, Black, Morris, Bryce 2003, Caulfield et al. 2004, WHO 2005).

The implications for future policy will be that improved diets and infant feeding practices at household level will be emphasized as part of child survival activities, but that distal aspects of undernutrition, including inequities such as the impact of globalization on the poor (Chopra & Darnton-Hill 2006, Darnton-Hill, Bloem, Chopra 2006), will need to be addressed in a realistic and overtly political way, if the goal is to be reached. Improving diets will automatically address most of the micronutrient deficiencies, including macroeconomic aspects (Darnton-Hill, Bloem, Chopra 2006, Darnton-Hill et al. 2006b). At this point, neither the implied WFFC goal for zinc (*'…and accelerate progress towards reduction of other micronutrient deficiencies…'*) (UN 2002b), nor the MDG1 are likely to be reached in the poorest countries. It has been estimated (UNICEF 2006b) that if progress towards achievement of target number 2 continues at the current inadequate rate, some 50 million children will not have their optimal nutritional status reached, with all the consequences this implies, including for micronutrient adequacy. The economic arguments are likely to be increasingly used and justified for investments in micronutrients as is starting to be seen by increased interest from the World Bank and the Bill & Melinda Gates Foundation.

As the public health importance of zinc has only relatively recently been recognized (as also demonstrated by the absence of a specific WFFC goal), there has been tremendous progress. On the other hand, a surprising amount remains relatively unknown: much more work and research is needed on zinc assessment, zinc and phytate content of local foods, simplified dietary methods and appropriate cut-off points for most age groups, aspects of zinc absorption and zinc intervention programmes (Hotz & Brown 2004, de Benoist et al. in press). Nevertheless, substantial efforts are underway to initiate programmes in developing countries (Caulfield et al. 2006), including delivery to recipients with other micronutrients.

7.4.2 Goal 2: Achieve universal primary education

Poor nutrition impacts on the education goal (MDG 2)- to achieve universal primary education- as it has been repeatedly shown to impair the ability of the poor to develop their skills, as well as later reducing the productivity of their labour (Pollitt et al. 1995,

FAO 2005, Grantham-McGregor et al. 2007). Iodine and iron deficiency and lack of breastfeeding during early childhood impair cognitive development (WHO 1999, SCN 2004, Lozoff 2006). Even poor children actually getting to school will be less able to take advantage of the opportunity if iodine deficiency, iron deficiency anaemia and other micronutrient deficiencies, low birth weight, stunting and inadequate young child feeding and nurturing practices are not addressed as all are associated with poor school performance later in the life of the child (Allen & Gillespie 2001, Pollitt et al. 1995, UNICEF 2005, Darnton-Hill et al. 2006b, Lozoff et al. 2006). Current hunger in school reduces attention span and school performance (UNICEF 2005).

The first years of life, including foetal life, are the most important periods in terms of mental, physical, and emotional development (Semba 2001). Iodine deficiency of the mother and hence during foetal life, has profound and irreversible effects on the child's mental capacity (Semba 2001, Hetzel et al. 2004). Even relatively mild iodine deficiency is associated with a reduction in IQ for a population. Iodine deficiency affects 15% of the population, causing almost 18 million babies a year to be born with their intellectual potential impaired. On-going deficiency in school children continues to lead to reduced cognitive function.

As noted, uncorrected iodine deficiency is only one of several factors negatively affecting educational attainment. School attendance and learning capacity both improve with improved nutrition (Caballero 2002, Li et al. 2003). Breastfeeding and adequate complementary feeding are seen as prerequisites for readiness to learn and significantly contribute to cognitive development. Reduced cognitive abilities correlate with anemia in both infants and school-age children with similar reduction in school performance (Jukes et al. 2002, Lozoff et al. 2006). More than fifty percent of school-age children suffer from iron deficiency anemia. Lack of stimulation and appropriate care can also lead to impaired intellectual development, and growth (WHO 1999).

Implications

MDG2: Although universal education might seem a relatively straightforward goal it has proven as difficult as any to achieve (UNDP 2005). As many as 113 million children still do not attend school, but the target is within reach for many countries, although not in all. India, for example, expected to have 95 percent of its children in school by 2005.

UNICEF estimates a somewhat higher figure of 121 million primary-school children out of school worldwide or which 65 million are girls (UNICEF 2004). In sub-Saharan Africa, at the current rate of progress, it will be well into the 22nd century before all children are in school. Some improvement in access to primary education and other areas has been more encouraging (UN 2006). Increases in Indian school enrolment had helped boost net enrolment ratios to 86 percent across the developing world, with the highest rates in Latin America where 95 percent of children are going to school. Rates are lagging in sub-Saharan Africa and need to improve in Oceania and Western Asia to meet the universal education goal, with fewer than half of all children in Burkina Faso, Djibouti, Eritrea, Ethiopia, Mali and Niger getting primary school education (UN 2006).

The iodine goal (*'Achieve sustainable elimination of iodine deficiency disorders by 2005…')* was not reached by 2005, although much progress was made, sometimes in the most challenging countries such as Nigeria. Nevertheless, 30% of households in countries affected by iodine deficiency do not use iodized salt and 86 million infants are born unprotected each year to mothers with inadequate iodine intakes. These figures are expected to improve when the findings from the UNICEF MICS surveys and USAID DHSS being done this year (2007) should give a better picture and are expected to show considerable improvement in many countries such as those in Eastern Europe (Mangasaryan et al. 2005, Untoro, personal communication 2007).

ICCIDD, along with UNICEF and the Network for the Sustainable Elimination of IDD, have developed a further strategy following the apparent failure to reach the WFFC goal, despite the quite amazing public health success of IDD elimination over the last 20 years. Constraints, as were seen in Chapter 6, to complete success of the elimination of IDD include: lack of adequate coordination and communication between sectors; a continuing need for advocacy, communications and training at all levels, insufficient quality assurance and monitoring, including strengthened laboratory management, and quality control and enforcement; and a remaining need to stimulate public demand an inattention to costs and to sustainability (Dunn 1996). International collaboration and private sector involvement remain critical aspects, as does addressing price differential and poor accessibility in some countries (Hetzel et al. 2004).

In its final report, the USAID-funded OMNI Project suggested a series of next steps and remaining issues for the two years before the end of the millennium (and beyond) (OMNI 1998). These seem to be just as pertinent today. For iodine these were: (i) strengthening of quality assurance and quality control of iodization programmes; (ii) accelerating existing programmes; (iii) eliminating pockets of IDD in unreached populations; and, (iv) ensuring sustainability of current programmes. One important aim will be for increased sustainability of USI with responsibility for iodization moving entirely to the private sector, with small salt producers a particular challenge. Nevertheless a strong governmental role will remain an essential ingredient in success in terms of facilitating legislation and monitoring and evaluation.

Again, general development and reductions in inequity will be important for any sustainable change, and in particular, addressing cultural and gender-based constraints against girls' education. One of the negative impacts of globalization has been a substantial reduction in public spending, particularly in the areas of education and health care to the poor (Lachapelle 2005, Darnton-Hill et al. 2005a, 2007). As discussed below, increasing the number of women educated will have positive intergenerational consequences for their children's nutrition and health (Smith & Haddad 2000, Smith et al. 2003). This pre-supposes these same women are adequately nourished in the first place and are not iodine deficient, so these two interventions, as with all interventions, need to go hand-in-hand, starting from before childhood (Darnton-Hill et al. 2006b).

7.4.3 Goal 3: Promote gender equality and empower women

While achieving each MDG is critical to development, two goals might be considered central to all others – universal education and gender equality/empowering women (UNDP 2003). Virtually all interventions to achieve all the goals interact with each other synergistically, in that improvement in one area of public health and nutrition will generally have a positive effect on other goals. This is particularly true of women's status and education (Smith & Haddad 2001) that affects women's health, including reproductive health, personal nutritional status and that of their children, and intergenerational effects through birthweight, iodine status, and iron status and so on.

Gender can negatively affect the nutritional status and health of girls, especially in South Asia (Mehotra 2004, Darnton-Hill et al. 2005b, UNICEF 2005). In turn, a woman's status impacts on the nutritional status of her child. Because women with higher status (relative to men) have better nutritional status themselves, they are better cared for and provide higher quality care to their children (Smith et al. 2003). Across countries, relative resources controlled by women tend to increase the share spent on education (Quisumbing & Maluccio 2000). Educated girls and women have fewer children, seek medical attention sooner for themselves and their children, and provide better care and nutrition for their children (Carnoy 1992, UNDP 2003). Women's empowerment helps raise productivity and to reduce infant mortality (UNDP 2006).

Poor female nutrition early in life reduces learning potential, increases reproductive and maternal health risks, and lowers productivity, and this intergenerational risk is then passed onto the daughters unless the cycle is broken. Multimicronutrients in pregnancy appear to be one way of increasing birth weights (SCN/WHO/UNICEF 2006). A recent review of social and economic costs of micronutrients and gender found them likely to be considerable (Darnton-Hill et al. 2005b), although overt discrimination in intrahousehold distribution likely plays only a small part in this, except in parts of South Asia (Mehotra 2004, Webb, Nishida, Darnton-Hill 2007). Nevertheless, the overall situation contributes to women's diminished ability to gain access to other assets later in life and undermines attempts to eliminate gender inequalities (Oniang'o & Mukudi 2002).

At a meeting held at WHO in Geneva on June 26-27, 2006, organized by the author and others, the results of randomized controlled trials assessing the impact on maternal micronutrient status and pregnancy outcome of multiple micronutrient (MMN) compared to iron/folic acid supplementation during pregnancy in developing countries were reviewed. Nine studies (conducted in Bangladesh, Burkina Faso, China, Guinea-Bissau, Lombok- Indonesia, Indramayu-Indonesia, Nepal, Niger and Pakistan) used the UNICEF/UNU/WHO (UNIMMAP) preparation containing 30 mg of iron and one RDA/RNI of the rest of the micronutrients (UNICEF/WHO/UNU 1999). The contents of the MMN supplements used in the other three studies (Mexico, Nepal, and Zimbabwe) varied slightly and the iron content was higher (60 mg). The review found that compared to iron/folic acid supplementation during pregnancy, supplementation with multiple micronutrients in developing countries had a small, statistically significant, consistent

and positive effect on mean birth weight of 22 gm (CI=11–33 gm). The risk of low birth weight (<2500 gm) was reduced with a relative risk of 0.91 (CI=0.84-0.99) in the MMN group compared to the iron/folic acid group. There appeared to be a small, non-statistically significant increase in mean infant length of 0.08 cm (CI=-0.02-0.18) and in head circumference of 0.09 cm (CI=0.00-0.17). There was no statistically significant effect on gestational age or rates of prematurity and there was evidence of statistically significant decreases in the prevalence in vitamin B and D deficiencies compared to the vitamin A control in Nepal (Sarlahi). Only one study was powered to assess perinatal survival, (Lombok, Indonesia). This study found a non-statistically significant reduction in the relative risk of perinatal mortality of 0.91 (CI=0.79-1.03). The relative risk of infant survival through 90 days was statistically significantly lower in the control group (iron/folic acid) at 0.81 (CI=0.70-0.95) compared to the MMN group. None of the other studies were powered to assess perinatal survival. However there are concerns of non-statistically significant increases in perinatal mortality in some settings (Christian et al. 2005 and refuting responses from Huffman, Habicht, Scrimshaw 2005 and Shrimpton et al. 2005) and this will currently have some programmatic implications, although a couple of countries (Indonesia and Pakistan) are likely to go ahead anyway and carefully monitor for any adverse effects. Meta-analyses are being conducted to assess the impact of MMN on perinatal mortality from all the studies. The resistance to these findings has been muted but consistent for reasons that are not entirely clear, as the cost-effective potential seems immense.

Implications

MDG3: There are some encouraging progress reports of progress towards gender equality and women's empowerment, but these tend to be high profile stories such as there now being eleven women Heads of Governments (in 2005). The proportion of seats in parliaments held by women is increasing, reaching about one third in Argentina, Mozambique and South Africa. However, for the vast majority of women in poor, and sometimes, not-so-poor, settings, progress in this goal has been very inadequate. Seventy percent of the 130 million children who are out of school are girls. Women account for two thirds of the 960 million adults in the world who cannot read; and of the world's one billion poorest people, three fifths are women and girls (UNDP 2006).

Increased knowledge and skills enable women to earn higher incomes, and thus enhance household food security, and education improves the quality of day-to-day care women give to their children (Darnton-Hill et al. 2005, Bushamuka et al. 2005). The positive association between maternal education and health and nutritional status of children is well established (Bicego & Boerma 1993, Smith et al. 2003, Chopra 2003). Improving both child and women's undernutrition is likely to be best achieved by empowering women and ensuring gender equality. This is most surely going to happen with increased levels of female education, protective legislation and greater control over assets. Conversely, improving nutrition will improve empowerment as girls with poor nutritional status are less likely to finish school. Given the already susceptible situation of women and girls in developing countries, attempts to improve the overall status of women through legislation and education should work hand-in-hand with attempts to improve the nutrition status of female girls, adolescents, and adults (Oniang'o & Mukudi 2002). Implications for policy and programmes are to increase female education and status. Improving micronutrient health is likely to be part of such interventions by improving health, education and reproductive health outcomes (SCN/WHO/UNICEF 2006). WHO already recommends universal distribution of iron (Fe) and folic acid (FA) supplements to pregnant women in developing countries to reduce iron deficiency anemia. Many women, however, face additional micronutrient deficits that can affect women's health, pregnancy outcome and infant survival, and so improving maternal micronutrient status is likely to be a major factor influencing the achievement of the Millennium Development Goals (Darnton-Hill et al. 2005b, SCN/WHO/UNICEF 2006).

7.4.4 Goal 4: Reduce by two thirds, between 1990 and 2015, the under-five mortality rate

This goal has perhaps the clearest relationship to micronutrients as both vitamin A and zinc are cited as preventive and curative interventions in reducing child mortality (Jones et al. 2003). As described in earlier chapters, vitamin A status reduces deaths from infectious diseases by on average, 23% in children in developing countries (Beaton et al. 1993). One of the three indicators for MDG4 is the under-five mortality rate (the others are infant mortality rate and proportion of 1-year-old children immunized against measles). Increasingly, vitamin A coverage is being included in the Child Survival Countdown process.

Poor nutrition and infant and young child feeding behaviours interact strongly with child mortality (Black, Morris, Bryce 2003). Almost half a million young children die each month from diseases such as diarrhoea and pneumonia, that in better circumstances would not be life-threatening, because of poor intra-uterine growth leading to low birth weight and continuing into early childhood due to inadequate feeding practices and a heavy disease burden. Exclusive breastfeeding alone is estimated to be able to save more than 3000 lives daily.

An estimated figure of over 60% of the nearly eleven million deaths among children under five is the proportion of childhood deaths that could have been prevented by interventions that are available today and are feasible for implementation in low income countries at high levels of population coverage (Black, Morris, Bryce 2003, PMNCH 2005). Breastfeeding and oral rehydration therapy (ORT) each are estimated to be able to prevent 13% - 15% of all under-five deaths respectively (Bryce et al. 2003). Continued feeding can be seen as part of the management of diarrhoea and other illnesses. Adequate complementary feeding could further reduce 6% of all under-five deaths (Black, Morris, Bryce 2003). If evidence level 1 or 2 interventions were universally available, 63% of child deaths could be prevented (Jones et al. 2003). Both vitamin A and zinc are at level 1 for diarrhoea prevention, level 2 for malaria prevention, and level 1 for zinc for pneumonia, level 2 for measles; and for treatment interventions, level 1 for measles for vitamin A and level 1 for diarrhoea for zinc (Jones et al. 2003). Based on such evidence, it has been estimated that among children living in the 42 countries with 90% of child deaths, this group of effective nutrition interventions could save about 2.4 million children each year (25% of all deaths) (Jones et al. 2003).

As has been demonstrated earlier, it is well recognized that in children with vitamin A deficiency, the risk of dying from diarrhoea, measles and malaria is increased by 20-24% (Beaton et al. 1993, Rice, West, Black 2004). The attributable fraction of these infectious disease deaths is higher in Sub-Saharan Africa, South Asia and Andean Latin America (Black, Morris, Bryce 2003). There is good evidence of the effectiveness of both vitamin A and zinc as both preventive and therapeutic interventions (Jones et al. 2003), leading to the prevention of over 2% of all deaths. Recent research on vitamin A and pregnancy outcome found that supplementing women of reproductive age with a weekly

low dose of vitamin A in Nepal significantly reduced maternal mortality in those mothers that became pregnant by 40% (West et al. 1999). These results need to be confirmed and research is currently underway in Bangladesh, Ghana and Nepal that aims to do this, although this does not appear to have been confirmed in the preliminary findings of the subsequent large study in Bangladesh.

Exclusively breastfeeding infants for the first four to six months of their lives benefit their health. Non-exclusive breastfeeding results in more than twofold increase in risks of dying from diarrhoea or pneumonia (Arifeen et al. 2001). Low birth weight often leads to child malnutrition and is directly related to the mother's health before and during pregnancy. Expanding access to reproductive health care and ensuring adequate nutrition enhance the health of both mothers and their children. Micronutrient deficiencies can be addressed through supplementation such as providing high-dose vitamin A capsules, by fortification such as the universal iodization of salt, or by improved dietary intakes through home gardens and other mechanisms, and by the reduction of social and economic inequities. Zinc supplementation also reduces mortality in small-for-gestational-age term infants that were supplemented with zinc from 1 to 9 months of age (Black 2003), and the potential role of antenatal multiple micronutrients have already been noted.

Implications

MDG4: At the current pace Sub-Saharan Africa would not reach the Goal for child mortality until 2165 (UNDP 2003). Because 90% of deaths occur in 42 countries, most of them in sub-Saharan Africa and in South Asia, and over 50% of global deaths occur in just six countries: India, Nigeria, China, Pakistan, DR Congo and Ethiopia (in decreasing order of magnitude), child survival programmes will become a major push in these and similar countries (PMNCH 2005). Already this is becoming an increased priority with donor countries such as Canada, Norway and the USA. Nearly two thirds of deaths in the 42 countries analyzed occur in just 19 countries where the predominant causes are pneumonia, diarrhoea, and neonatal disorders. It has been suggested that classifying underweight status and micronutrient deficiencies as underlying causes of death if followed by the infectious diseases that are the terminal associated causes would help to underline the importance of undernutrition in half of all deaths in children under five

years of age (Scrimshaw & San Giovanni 1997, Shankar & Prasad 1998, Pelletier & Frongillo 2003, Caulfield et al. 2004).

As seen from previous experience, many countries made substantial progress in reducing child mortality over the 15 years following the launch of the Child Survival Revolution in 1982. The average number of under-5 deaths fell from 117 per 1000 in 1980 to 93 per 1000 in 1990 (UNICEF 2001). Unfortunately since the mid-1990 gains in child survival have slowed or been reversed. The child summit goal for the 1990s – reducing child mortality by a third or to less than 70 per 1000 – remained far from being achieved. Instead of a 33% reduction, worldwide under-5-years mortality declined from 93 deaths per 1000 in the early 1990s to 82 per 1000 in 2002 (UNICEF 2001). If trends in under-five mortality rate during the 1990s continue at the same rate until 2015, the reduction of mortality globally over the period 1990-2015 will be about one quarter, far from the goal of two thirds reduction (WHO 2005a). As the same report notes, even 'if the rate of reduction increased fivefold, the goal of a two thirds reduction would still not be reached by 2015.' (WHO 2005a). Clearly one of the constraints is how to maintain political will both in countries and within international agencies, but especially the donors. There is increasing evidence that this is happening with funding flows, an expanding evidence base, and coalitions such as the Partnership for Maternal, Neonatal and Child Health and internal agency workplans.

Programmatically, a mix of interventions will give governments the chance to shift from a subsidized vitamin A capsule programme to more sustainable, non-subsidized Government-funded vitamin A interventions. In an appreciable number of countries, supplementation with vitamin A will be a necessity for some years to come, but it is likely to increasingly become part of child survival interventions. Fortification, except in Central America and the industrialized countries, is yet to prove itself as an effective alternative in improving population vitamin A status but is receiving increased attention again.

Issues over the next few years are likely to include: (i) transitioning from reliance on stand-alone universal supplementation to a mixture of child survival based interventions such as Child Health Weeks, as well as fortification, other food-based approaches and targetted supplementation; (ii) supporting provision of high dose vitamin A to mothers

within 8 weeks of delivery (which is currently seeking a stronger evidence base as to its benefit to infants); (iii) addressing women's nutrition and health, including micronutrient status, leading to a life-cycle approach; (iv) identifying and using other EPI mechanisms as well as routine health service delivery for vitamin A after the polio eradication campaign is complete, such as the Accelerated Child Survival and Development programme in West Africa (UNICEF 2004); (v) studying the form and dosage regimen of supplements (retinol or beta-carotene, smaller intakes weekly, or daily as a component of a multi-micronutrient supplement, or 200,000IU, every four to six months); and, (vi) assessing whether there is a role for vitamin A in malaria case management and mitigation (OMNI 1998, West & Darnton-Hill 2001, Dalmiya, Palmer, Darnton-Hill 2006).

7.4.5 Goal 5: Improve maternal health

Several micronutrient deficiencies (iron, vitamin A, folate, iodine, calcium) are associated with pregnancy complications. One tenth of maternal mortality in developing countries is attributable to iron deficiency, causing the deaths of more than 60 thousand women a year in pregnancy and childbirth. Poor nutrition also impacts negatively on maternal health (MDG 5) as childhood stunting increases the risk of obstructed labour later in life, leading to increased maternal mortality. Undernutrition and anaemia of girls and women contribute significantly to maternal morbidity and mortality and to low birth weight infants (Brabin, Hakim, Pelletier 2001). The importance of maternal iron-deficiency anaemia as a contributory factor to maternal death was first highlighted decades ago (Harrison 1975) and now recognized to be a contributing factor in 20% of all maternal deaths (WHO 2001, Stoltzfus, Mullany, Black 2004). Iron interventions to reduce severe iron deficiency anaemia can be expected to reduce maternal mortality considerably (WHO/UNICEF 2005). Obstetric complications however are the major cause of death among women of childbearing age, far ahead of tuberculosis, suicide, sexually transmitted diseases or HIV/AIDS (IAGSM 1998). In developing countries, on average, every second pregnant woman is anaemic, mainly due to iron deficiency (WHO 2001).

In terms of the earlier goals of reducing poverty and improving education, iron deficiency and anaemia reduce the work capacity of individuals and entire populations, bringing serious economic consequences and obstacles to national development (Alderman &

Horton 2007). The most vulnerable, the poorest and the least educated are disproportionately affected by iron deficiency, while later physical and cognitive development is impaired, resulting in lowered school performance- a vicious cycle within the poverty cycle. Reducing severe iron deficiency anaemia, and other micronutrient deficiencies, will be a small part towards reducing maternal mortality, as the greater gains will need to be made in improved health systems, female education and improved obstetric care.

At the same time, as previously noted, although the most prevalent of the three deficiencies, the prevention and control of iron deficiency anaemia has been the least successful, even though the goal was also the most modest. Consequently the WFFC goal **('…***reduce by one third the prevalence of anaemia, including iron deficiency, by 2010…')* is not likely to be reached. Almost ten years ago, the Sub-Committee on Nutrition of the UN system drew attention 'to the lack of progress in tackling iron deficiency anaemia despite its affecting the health and development of tens of millions of children and women in spite of the availability of practical low-cost interventions' (ACC/SCN 1997). Constraints are multiple, starting with the fact that it is a harder problem to tackle programmatically. However, it has been of lesser priority, logistics remain complicated, compliance is often low, bio-availability in the diet, especially in the diets of the poor, is low, and further reduced in many largely vegetarian diets, and the status is worsened by coexisting conditions of parasite infection and malaria.

Implications

MDG5: The already high maternal mortality rate is increasing in many countries. Although some countries have experienced reductions in maternal mortality, such declines have not occurred in countries where pregnancy and childbirth are most risky (WHO 2005a, b). Sub-Saharan Africa accounts for half of the developing world's maternal deaths, with one of every 100 live births resulting in the mother's death and every year more than 500 000 women die in pregnancy and childbirth. A pregnant woman is 100 times more likely to die in pregnancy and childbirth in Sub Saharan Africa than in a high-income OECD country (UNDP 2003). In the developing world, while the risk of dying in childbirth is one in 48, virtually all countries now have safe motherhood programmes.

The over-riding implication is that effective antenatal and improved status of iron and other micronutrients needs to be rapidly scaled-up throughout the life-cycle, both for improved development and work capacity but also so that young women go into their first pregnancy with adequate iron and micronutrient stores. Therefore the next steps suggested for iron should include: (i) expanding fortification of flour and other foods with iron and folic acid and other B vitamins and possibly zinc, and this is well underway (there are now two non-governmental bodies promoting fortification- GAIN and FFI), as well as an increased priority for Agencies; (ii) increasing emphasis on iron deficiency anaemia and other nutritional anaemias (Kraemer & Zimmermann 2007) as the other two main micronutrients show progress, including through increased use of multimicronutrient supplements, both in children and pregnant women; (iii) promoting a life-cycle approach targetting adolescents so that young women enter their first pregnancy with adequate micronutrient status, and including identifying the most appropriate paediatric formulation for infants and children in poor circumstances such as home-based fortification with micronutrient powders, (e.g. 'sprinkles'), dispersible tablets (e.g. 'foodlets') and fortified supplementary foods such as 'plumpy nut'; (iv) using other delivery mechanisms- schools, factories, private sector outlets; (v) clarifying the efficacy and effectiveness of weekly vs. daily dosing (WHO has recently held a Global Expert Consultation on this in the Western Pacific Regional Office); (vi) improving logistics (procurement, distribution, delivery systems); (vii) modifying iron supplements to improve acceptability (taste, odour, side effects, packaging, and brand names); and, (viii) advocating the cost-effectiveness with regard to the health and productivity-increasing effects of interventions. A further development is likely to be a regional approach to fortification in terms of exports and imports, harmonization of standards and common legislative approaches, building on the common ground of Codex Alimentarius, especially in an environment of economic globalization, while ensuring protection of national Governments to make their own public health regulations (as specified in the WTO regulations but currently open to potential abuse).

7.4.6 Goal 6: Combat HIV/AIDS, malaria and other diseases

This particularly ambitious goal has as two of its targets- to have halved by 2015 and begun to reverse the spread of HIV/AIDS and to have halted by 2015 and begun to reverse the incidence of malaria and other major diseases. Discussion of possible

varied, and still to be elucidated, interactions between micronutrients and these global diseases is beyond the scope of this chapter but will clearly be important in the future programming, although will be only part of an integrated approach. Already the findings of a possible adverse effect of iron supplementation on young children in malaria-endemic areas (Sazawal et al. 2006) have prompted the need for a WHO Expert Consultation and a consequent UNICEF/WHO Meeting (the latter in Nairobi and organized by the author). Poor nutrition also impacts on HIV/AIDS and malaria, as it hastens the onset of AIDS among HIV-positive individuals, and reduces malarial survival rates. Undernutrition may also compromise the efficacy and safety of ARV treatment, and weaken the resistance to opportunistic infections. It is increasingly understood that malaria needs an integrated approach with anti-malarial treatment and prophylaxis, impregnated bednets, water, sanitation and environmental interventions, and adequate and appropriate nutrition, especially of micronutrients, as well as treatment of accompanying disease. HIV is an even more complex disease condition, both physiologically and politically and these factors are played out in the nutrition arena as well. Reference will be made to recent reviews on the topics of HIV and nutrition (Semba & Gray 2001, Singhal & Austin 2002, Friis 2006, Drain et al. 2007, Villamor, Fawzi, Msamanga, in press) and malaria and nutrition (Shankar 2001, 2007, Prentice et al. 2006), but a detailed review is not within the scope of this chapter. However, some implications are addressed below. The current WHO booklet on HIV and Nutrition is programmatically not very helpful and plans are underway to update it (WHO 2003).

Undernutrition affects both the body's immunological and non-immunological defenses. As a result, it increases the incidence, severity, and duration of common childhood diseases, such as diarrhoea, acute respiratory infections and measles, as well as exacerbating malaria and considerably increasing the likelihood of mortality (Shankar 2001). In the pathogenesis of HIV infection nutritional deficiencies may play a role as anti-oxidants and in immune function. There is an association of deficiencies of micronutrients in HIV-infection with immune deficiency, rapid disease progression, and mortality (Semba & Gray 2001). In children with vitamin A deficiency, the risk of dying from diarrhoea, measles, and malaria is increased by 20-24% (Ezzati et al. 2003). Zinc has a role in malaria prevention and control (Shankar 2001, Jones et al. 2003), as does vitamin A, the B vitamins such as folate, riboflavin and thiamin, as may vitamin E and other anti-oxidants (Shankar 2001).

In the ground-breaking observational study of Semba et al. (1994), low plasma levels of vitamin A were found to be associated with higher risks of HIV and infant mortality (Semba et al. 1994). However, supplementation studies have not shown the positive effect that might have been expected (Semba & Gray 2001) and recent studies (e.g. those of Humphrey et al. (2006) have further complicated the picture. Vitamin A supplementation can mitigate the adverse effects of HIV infection, malaria, and diarrhoea on child growth and morbidity (West & Darnton-Hill 2001, 2007, Villamor et al. 2001) but has little impact on transmission (Semba & Gray 2001). Weekly supplements given to women of reproductive age have been shown to improve birth outcomes and health of infants born to HIV-positive mothers (Coutsoudis et al. 1999). Fawzi has recently suggested that the 'benefits of vitamin A supplementation in pregnant women and their infants 'may be offset in HIV-infected women by an adverse influence of such supplementation on HIV transmission and disease progression (Fawzi 2006). Recommendations on infant feeding have recently been updated in terms of the prevention of mother-to-child transmission and will be published shortly.

Much research is currently underway with both HIV and malaria prevention and control, and the appropriate role for micronutrients, and nutrition in general. In a clinical trial with HIV-positive men and women in Miami selenium supplementation led to a 62% reduction in admission rates and hospitalizations due to infections compared to the placebo group. There is a suggestion that selenium reduces the progression of HIV/AIDS (Semba & Gray 2001). Drain et al. (2007) have reviewed, as have others before them (e.g. Semba & Gray 2001) the possible roles of other micronutrients. What does seem clear is that populations with high levels of HIV infection are also often at risk of deficiencies of more than one micronutrient.

Importantly, research in Tanzania shows that multiple micronutrient supplements significantly improved pregnancy outcome in HIV-positive women (Fawzi et al. 1998, Fawzi et al. 2004b). In HIV-positive women, multivitamin supplementation reduced by 44% the risk of low birth-weight, and reduced significantly foetal death, pre-term birth and small size for gestational age, plus positively affecting a number of indicators of immune function, although using a very different formulation (Fawzi et al. 1998). Vitamin A alone did not have a significant impact on these factors (Fawzi et al. 1998)

and may even have a slightly negative impact on some aspects (Fawzi et al. 2004a). On the other hand, vitamin A supplementation in children with HIV may accelerate their growth. Vitamin B12 may slow HIV immune deficiency disease progression and reverse neurological compromise (Tang et al. 1997), but the role of micronutrients in HIV/AIDS prevention and control is still unclear (Semba & Gray 2001) although continued research shows promise, at least in reducing side effects and sequelae (Fawzi et al. 2004). Unfortunately, as was noted, the exciting work by Fawzi's group (Fawzi et al. 1998, 2004) used a somewhat idiosyncratic dosing regime of vitamins, with up to eight times the RDA/RNI of some of the constituent vitamins, and except in Tanzania has not been picked-up as a public health intervention. The clearest conclusion at present seems to be that it is important for those at risk, and those infected, to be as optimally nourished as possible, while therapeutic uses of micronutrients in HIV and malaria remains uncertain, but promising.

Implications

MDG6: Depending on the indicator used, progress is inadequate with some encouraging signs although less so in sub-Saharan Africa where HIV prevalence rates among adults have reached around 7.4%, rising to over 20% in some countries in the sub-region. On the other hand prevalence rates appear to have stabilized in most sub-regions (as opposed to some individual countries) in sub-Saharan Africa. Eastern Europe is of concern and countries of Asia and the Pacific are showing increases. Some countries have shown the epidemic can be checked by a strong response, for example countries like Brazil, Senegal, Thailand and Uganda have shown that the spread of HIV can be stemmed (WHO 2005). Just under half of the people living with HIV are female (57% in sub-Saharan Africa).

At a minimum 1 million people die of malaria each year and it is a likely contributor to death in another 2 million deaths. There is little progress in these rates, although there are some encouraging features such as the increase in use of bed rates, which by 2003 had increased 4-fold in sub-Saharan Africa in 5 years, and the considerably greater amounts of funding available for malaria and HIV over the last few years has already shown further increases in bednets and other malaria control uptake (WHO 2005) and these funding increases are even accelerating.

Nutrition will have a role in the prevention and control of both diseases, including others like tuberculosis, but as adjuncts. Undernourished populations, including inadequate intakes of micronutrients, are at generally higher risk of getting the diseases and progression is generally also faster. The role of micronutrients in treatment of HIV, but not as a substitute for ARVs, remains unclear, but the levels used by Fawzi et al. (2004) are, as already noted, several times the RDIs, and so if having an impact it may well be pharmacological rather than nutritional. The poor diets that women in developing countries consume due to poor availability and limited consumption of micronutrient rich foods, lead to deficiencies of iron, vitamin A, zinc, folic acid, B6, B12 and occasionally other vitamins and minerals. Such deficiencies have important consequences for women's own health, pregnancy outcomes and their breast-fed children's health and nutritional status (Huffman et al. 1998). UNICEF has recently recommended that a combined vitamin-mineral supplement for pregnant women is a cost-effective option that needs to be considered for developing countries in the absence of any other treatment while ARVs become available and established and WHO/UNICEF have issued a guidance recommending the use of multimicronutrient supplements in such situations for HIV positive women and infants and children of infected mothers, at the level of one RDA/RNI.

Increasing coverage of affected populations with improved nutrition, including the appropriate micronutrient formulation, will continue to be a primary objective of country programmes, and may become a focus of the donors involved, but ARVs will rightly be the main emphasis, and behavioural change. This is being done by expanding and developing non-traditional modes of delivery- through EPI, the private sector, schools, and differing regimens to improve compliance and cost and so on. Cost effectiveness of different interventions and availability of ARVs will increasingly be used to guide country choices on appropriate intervention strategies. The main constraints to scaling-up relate to inadequate health systems and supply provision and quality assurance. Another constraint might be the current uncertainty around giving iron or iron-containing supplements to children in high malaria endemic areas following the findings of Sazawal et al. of increased adverse events and mortality in children given iron supplements in an RCT in Pemba on Zanzibar in Tanzania (Sazawal et al 2006). However, it appears likely that these results apply only in such environments as such results were not found in a similar study in Nepal (Tielsch et al. 2006). A questioning comment from the Kenya

Medical research Institute/Wellcome Trust Collaborative programme (English & Snow 2006) and an earlier article from the same setting showing that low-dose daily iron supplementation for 12 months did not increase the prevalence of malarial infection or density of parasites in young Zanzibari children (Mebrahtu et al. 2004), a finding mirrored by the sub-study of the Pemba trial where increased survival was found in children treated with anti-malarials, iron and treatment of infectious diseases (Sazawal et al. 2006). The role of the folic acid in the supplementation of the treatment group is also attracting increasing critical concern, especially as the anti-malarials at the time were folate anti-metabolites (English & Snow 2006).

There will also likely be more involvement of the private sector in sale of supplements. Particularly with donor encouragement, there will be some emphasis on using the private sector as the avenue for supplements, as in the recent experience in Indonesia. A recent survey in the Philippines found that while around 90% said they would be willing to buy supplements most would not spend more than 20 pesos (about 5 US cents) on iodized oil or vitamin A supplements, citing a lack of money and a feeling that it was the government's responsibility. A recent report by Cavalli-Sforza et al. (2005) showed that iron/folic acid supplements could be cost-effectively distributed through a combination of the private sector with social marketing and the public sector health system.

7.4.7 Goal 7: Ensure environmental sustainability

These final two goals are less directly concerned with micronutrients, though of enormous importance (not achieving goal 7 may make all the others irrelevant), and so will here receive less attention. One target for this goal is to have, by 2020, achieved a significant improvement in the lives of at least 100 million slum dwellers, but one of the indicators is the proportion of households with access to secure tenure (owned or rented) which would be very applicable to poor farmers and rural households and both have implications for household food and nutrition security.

Given the apparently increasing frequency of natural, and man-made, emergencies, it is of relevance that in 2005, in response to the Tsunami emergency, a joint statement was developed and disseminated by WHO, WFP and UNICEF on the need to provide multiple vitamin and mineral supplements for these vulnerable groups affected by

emergencies. Several 'emergency' countries have since then initiated the distribution of multiple vitamin and mineral supplements to pregnant and lactating women including Indonesia and Niger. The use of paediatric formulations in powder form (e.g. 'Sprinkles') has been initiated in Indonesia and they are increasingly being considered by other countries as part of emergency response (de Pee et al. 2007).

Implications

MDG7: More than one billion people still lack access to safe drinking water and more than two billion lack sanitation. The implication for nutrition, although less so for micronutrients apart from zinc, is the impact of this on morbidity and mortality of children, especially from diarrhoeal diseases. During the 1990s, however, nearly one billion people gained access to safe water and the same number to sanitation. In 2002, some 1.1 billion people, one sixth of the world's population, still lacked access to improved drinking water, the majority being in Asia and Africa. Urban-rural disparities remain a problem and are greatest in sub-Saharan Africa where only 45% of the rural population has access compared to 83% in urban populations and similar levels of disparities occur in parts of Latin America (WHO 2005). The overall progress seen in the period 1990-2002 of around one third reduction in the percentage without access shows that the MDG goal is attainable if the current rate of progress is sustained (WHO 2005). However, sub-Saharan Africa is unlikely to reach the target (WHO 2005). Using the indicator for access to improved sanitation, urban and rural, the goal is unlikely to be obtained even with considerable acceleration (WHO 2005).

7.4.8 Goal 8: Develop a global partnership for development

Although some of the earlier goals would seem to have more direct impact on health and child survival, it has been argued that this goal, if achieved (and current discussions are not encouraging), could have the greatest impact on health and well-being, adequate nutrition, including of micronutrients (found more often and in a more bio-available way) in diets beyond those characterized as diets of poverty, where the micronutrient content and quality of the diets are far less likely to be adequate. The targets include critical distal factors such as: 'Develop further an open, rule-based, predictable, non-discrimatory trading and financial system' which includes 'a commitment to good

governance, development and poverty reduction- both nationally and internationally (with level of official development assistance as the indicator). Target 13 is to address the special needs of the least developed countries including tariff and quota free access for the least developed countries' exports; enhanced programme of debt relief for heavily indebted poor countries and cancellation of official bilateral debt; and more generous overseas development aid (ODA) for countries committed to poverty reduction. What has been an emerging trend is the emphasis on public private relationships (see Chapter 4) and the increase in private foundations with international health as a high priority e.g. the Bill and Melinda Gates Foundation. Nevertheless, this has not always meant more total funds for international health in some areas, including nutrition, although this appears to be changing, even if mainly at level of debt forgiveness at this point.

Implications

MDG8: One of the indicators concerning affordable essential drugs on a sustainable basis has obvious relevance, especially when multimicronutrient supplements are added to the list (and available through the UNICEF Supply Division in Copenhagen). Considerable progress continues to be made. The private foundations interest in this area will undoubtedly assist, and there appears to be considerable support for a fairer approach by the pharmaceutical companies, some of who have been searching for ways in which their goals, and the public health nutrition goals can be mutually reached (while remaining different by definition of desired short-term outcomes, at least). A major boost occurred when in 2001, the WTO ruled that the TRIPS (Trade Related Aspects of Intellectual Property Rights) agreement, which protects patents on drugs, should be interpreted to support countries' rights to safeguard public health and promote access to medicines for all (WHO 2005), although poor countries' access to the legal process remains constrained. There will be increasing emphasis on getting more funds for nutrition through the PRSP mechanisms of the World Bank, through SWApS and through nutrition and micronutrient activities coming in under child survival and related activities. Although there has been some debt relief, the hoped for increase in funds because of the near-universal adoption of the MDGs has not yet happened. As one aspect of this goal is partnerships, there are some encouraging signs that global nutrition players (see Chapter 4) may at last be recognizing that to get adequate global attention and resources, they must speak with one voice (Darnton-Hill, Bloem, Chopra 2006).

7.5 Overall progress

It is now firmly established that over half of all childhood deaths in the developing world have undernutrition, including micronutrient deficiencies, as the underlying cause. The elimination of vitamin A deficiency and the iodine deficiency disorders, and the substantial reduction of iron deficiency anaemia have been endorsed as achievable goals by virtually all countries of the world. The cost effectiveness of most micronutrient interventions continues to need advocacy to policy makers but has an increasingly strong evidence base (e.g. the Copenhagen Consensus 2004). Overall, the early estimates of "for less than 0.3% of their GDP, nutrient deficient countries could rid themselves of these entirely preventable diseases, which now cost them more than 5% of the GDP in lost lives, disability and productivity" (McGuire & Galloway 1994), has been useful for advocacy but the economic arguments need to be more widely internalized in health policies and planning.

Human development and decreases in international inequities, as a whole are, however, proceeding too slowly (UNDP 2003 amongst others). Some 54 countries are poorer now than in 1990. In 14, more children are dying before age five. In 12 countries, primary school enrolments are shrinking. In 34 countries life expectancy has fallen. Such reversals were previously rare but were noted in the mid 1990s for nutrition (ACC/SCN 1997) and were due to largely political decisions, encouraged by donor Governments and the World Bank policies (Lancet 1994). A further sign of a development crisis is the decline in 21 countries in the human development index (HDI), a summary measure of three dimensions of human development – living a long and healthy life, being educated and having a decent standard of living. This decline was rare until the late 1980s, for reasons already alluded to, because the capabilities captured by the HDI are not easily lost (UNDP 2003).

Concerns have been raised that current global levels of investment and implementation for child health activities are inadequate and the international community will therefore not meet the child health MDGs, even though a number of simple, proven child survival interventions are available (Sachs 2001, Bryce et al. 2003). Of the measurable health Goals, the world is farther from achieving the one for child mortality – a two-thirds reduction by 2015 - than any other (UNICEF 2004).

If progress does not accelerate, it will take more than 100 years for some regions to achieve some of the Millennium Development Goals (UNDP 2003). That so many countries around the world will fall short of the MDGs in the eight years to 2015 points to an urgent need to change course (UNDP 2003). The most recent U.N. progress report on the goals found that while global incidence of extreme poverty has declined, some 140 million more people have entered that category in sub-Saharan Africa. More people are also going hungry in the region, which, according to the study, has seen only modest improvements in child mortality and maternity mortality rates in the past six years. "Disparities in progress, both among and within countries, are vast and ... the poorest among us, mostly those in remote rural areas, are being left behind." (UN 2006). Although several countries have successfully reduced HIV infection rates, in line with the goal to halt and begin to reverse the spread of the disease that causes AIDS by 2015, infection rates are increasing globally and the number of people living with the disease continues to rise. The report said that distribution of insecticide-treated mosquito nets to combat malaria has increased ten-fold in sub-Saharan Africa, but their use varied between richer and poorer populations, and city and rural dwellers (UN 2006).

What more could be done (Darnton-Hill 1999a)? That virtually all affluent donor countries' levels of international aid are currently less than 0.3% of their GNP is a disgrace and should be an embarrassment, particularly against earlier commitments to aim for at least 0.7% of GNP, and with countries like the Netherlands and Norway regularly achieving 1%. The US, while a major donor in cash terms is less than 0.1%- and even of that the US State Department itself claims 90% is spent in the US itself.

The gap remaining in research, technical and programmatic leadership, especially in iron deficiency anaemia needs more attention and funding. The dearth of funds from the private sector for diseases of the developing world is regularly noted. It has been noted that less than 10% of research funds are spent on diseases that affect 90% of the burden of disease. Without care, current globalization trends will exacerbate this, as seems to be happening for the very poor (World Bank 2006), even when average indicators of MDG progress are improving in a country (Moser, Leon, Gwatkin 2005). WHO has recently been addressing this with innovative partnerships, but the mechanisms, and benefits, are still being worked out. For example, WHO and WTO have recently co-published a book recognizing the potential negative impact of some

WTO regulations and how these might be mitigated. Due of such gaps, private foundations such as the Bill & Melinda Gates Foundation, are increasingly defining the global health agenda (and are currently negotiating with UNICEF and GAIN a large investment to complete the universal salt iodization agenda).

As the past chapters have demonstrated, there has been considerable progress towards eliminating micronutrient malnutrition, especially in addressing the iodine deficiency disorders and vitamin A deficiency but less so with iron deficiency anaemia. Increased cooperation between governments, communities, the food industry, agriculture and academia will be needed. The exact mix and sequencing of interventions, and when to modify these, will become the important questions for each national programme. Complementary approaches of nutrition education, fortification, dietary diversification and appropriate supplementation together, are most likely to ensure impact and sustainability. A major challenge at present is to make the elimination of micronutrient malnutrition more consumer-driven and community-based (Allen & Gillespie 2001). On-going national commitment remains an issue, despite demonstrated cost-effectiveness of micronutrient interventions, not least because of competing needs such as the HIV/AIDS epidemic. As accepted by the Group of 8, at Monterey for example, more funds are needed. At the very least, donor countries should fulfill funding promises already made. The current experience of the Global Fund for AIDS, Tuberculosis and Malaria is not encouraging. If special efforts are not made to tackle these global nutrition problems, the achievement of the elimination of micronutrient deficiencies, the WFFC goals and most MDGs will be seriously compromised.

One of the original questions implied in this thesis was whether the following UNICEF World Fit for Children micronutrient goals would be reached?
"Achieve sustainable elimination of iodine deficiency disorders by 2005 and vitamin A deficiency by 2010; reduce by one third the prevalence of anaemia, including iron deficiency, by 2010; and accelerate progress towards reduction of other micronutrient deficiencies, through dietary diversification, food fortification and supplementation".

The answer is known for one- the iodine deficiency disorders goal of 2005 was not reached although considerable progress was made. It is also unlikely the other goals will also be reached, and it is unclear whether much progress at all will be made on iron

and anaemia, although progress is looking somewhat more optimistic than it was. Nevertheless, considerable progress has been made both in terms of more accurate prevalence figures and also in terms of new knowledge, new approaches, strengthened evidence bases and a continuing determination that this is one area of public health where progress is possible, increasingly as integrated approaches and using other partners while encouraging country ownership. As has been made clear in this chapter, the MDGs are now the more important goals, an event that would not have been predicted in 2000 when the new UN goals for children were being planned. As nutrition is in the main only indirectly addressed by these, and micronutrients only implicitly, it is important that the opportunity is not lost because they are not being measured. It is the challenge for the public health nutrition sector to ensure that success is measured in a way that the real contribution to reducing or eliminating micronutrient deficiencies is recognized and encouraged and the larger impact of this towards improving health and development and the global goals acknowledged.

Table 7.1

Contribution of nutrition, including micronutrients, to achieving the MDGs

MDG Goal	Goals	Contributions of Nutrition (adapted from SCN 2003)
1	**Eradicate extreme poverty and hunger**	Substantial and strong evidence that malnutrition increases the risk to disease and decreases the ability to respond, impairs physical and intellectual potential of functioning and hence economic productivity- this is true of some micronutrients that may be limiting of both growth and intellectual functioning e.g. iodine, iron and zinc. Household food security improvement, particularly in HIV/AIDS affected families and communities will be crucial.
2	**Achieve universal primary education**	School attendance and learning capacity both improve with improved nutrition of the pre-school and school-age child, particularly children affected by HIV/AIDS. Breastfeeding and adequate complementary feeding are prerequisites for readiness to learn and significantly contribute to cognitive development. Maternal iodine deficiency reduces intellectual capacity of her child. Sustained iron deficiency anaemia impairs cognitive development.
3	**Promote gender equality and empower women**	Improving nutrition, including reducing anaemia, amongst adolescent girls and pregnant and lactating women is a prerequisite to improve women's physical and mental capacity and their ability to participate as equal citizens. The necessary capacity development for nutrition empowers women and enhances their participation in society.
4	**Reduce childhood mortality**	Infant mortality could be readily reduced by 15% with improved breastfeeding practices alone. 60% of young child deaths are associated with malnutrition, greatly caused by inadequate complementary foods and feeding together with poor breastfeeding practices. Reduction by two-thirds of under-five mortality necessarily requires the rapid improvement of young child feeding practices. Vitamin A and zinc, as well as iron and likely other micronutrients, are important to enhance immuno-competence and reduce deaths from diarrhoea and respiratory diseases in infants and children.
5	**Improve maternal health**	Undernutrition and anaemia of girls and women contribute significantly to maternal morbidity and mortality and to low birth weight infants. Significant improvement in macro and micro nutrient status of girls, adolescents and women is urgently necessary. Increased attention is needed to support mothers' nutritional and social needs. Breastfeeding also contributes to reduced iron losses and to the duration of birth intervals, reducing maternal risks of pregnancy too close together.
6	**Combat HIV/AIDS, malaria and other diseases**	Undernutrition may enhance susceptibility to HIV infection and certainly accelerates the progression from HIV to AIDS and greatly increases AIDS mortality. Moreover, undernutrition and micronutrient malnutrition decrease the likelihood of successful compliance with treatment that reduces the likelihood of drug resistance. Nutrition

		improvement and support are key to reducing the impact of the epidemic, and also may increase effectiveness /safety of ARV's. Women with low vitamin A status have increased transmission of the virus (although supplementation does not reduce this). Vitamin A in children and multimicronutrients in pregnant women have shown to reduce symptoms or delay progression of the HIV to AIDS. Exclusive breastfeeding in an otherwise untested population could be associated with as much as a 15-20% reduction in MTCT. Undernutrition has long been recognized as a major factor in both TB incidence and morbidity. A major effort to improve nutrition must accompany the DOTS strategy.
7	**Ensure environmental sustainability**	Environmental sustainability requires active community demand and involvement and the involvement of many sectors. Community based nutrition programmes contribute to awareness of the need for water and a clean environment and also build community capacity and involve sectors crucial to environmental improvement. Home gardening, besides increasing micronutrient intake may also help environmental sustainability
8	**Develop a global partnership for development**	The activities called for in achieving the micronutrient goals and various NGOs and Global Funds such the Micronutrient Initiative and GAIN, as well as the Global Strategy on Infant and Young Child Feeding help direct attention to micronutrient needs and programmes as well as increased attention to support for the mother's nutritional and social needs.

Chapter Eight

Conclusions

8.1 Aims

The first aim of this thesis was to identify constraints and facilitating factors contributing to the success, or otherwise, of achieving the first set of international micronutrient goals by the stated date of the end of the previous decade (2000) (UNICEF 1990). In the course of writing the thesis, another set of UN micronutrient goals were endorsed (UNICEF 2002). However, it has become apparent that the Millennium Development Goals (MDGs), which do not explicitly mention micronutrients, are now, and will be, driving the international health and nutrition agenda, at least until 2015 (UN 2000 a,b,c, 2001, 2002b). The programmes and policy decisions used in addressing micronutrient malnutrition have however not fundamentally changed, although their positioning has again been modified with the Child Survival approach that has become the current paradigm in international health (Lancet 2003). This follows the World Health Report (WHO 2002, Ezzati et al. 2002) and the Lancet series of articles from the Bellagio Child Survival Study Group, and subsequently expanded to the Partnership for Maternal, Neonatal and Child Health (Bellagio Child Survival Study Group 2003, PMNCH 2005), with a prominent role for vitamin A and zinc. Although there is good evidence of an impact of iodine status on child survival (Cobra et al. 1997, Semba 2001a), it is not explicitly mentioned. Iron deficiency is also not seen as a priority, although the Copenhagen Consensus rated it the second most cost-effective global intervention (Copenhagen Consensus 2004).

Vertical initiatives such as the Global Alliance to Improve Nutrition (GAIN), the Flour Fortification Initiative (FFI) and the International Council for the Control of Iodine Deficiency (ICCIDD) and others have all helped to increase interaction with the private sector, especially with fortification, including the continuing global IDD elimination goal through the iodization of salt. Other non-Governmental organizations (NGOs) such as The Micronutrient Initiative (funded largely by the Canadian CIDA) and USAID

micronutrient programmes (VITAL, OMNI, MOST and currently A2Z) have played important roles, subject to policy shifts by their bilateral funders, along with other Governments such as Australia and the Netherlands. However, the factors that facilitate or constrain programmes do not seem to have changed so much, whereas the application of such programmes and the funding may have. While the Millennium Development Declaration and Goals have become the overarching global goals (UN 2001, 2002b, World Bank 2004, WHO 2005), the earlier goals continue to be the basis for work planning and implementation (UNICEF 1990, FAO/WHO 1992, UNICEF 2002). UNICEF's most recent four-year Medium Term Strategic Plan (MTSP 2006-2009) for example, explicitly uses the MDGs in its five focus areas, and hence in the results to be reached in each of these focus areas, while planning continues along the lines of each micronutrient and infant and young child nutrition. Reflecting the above shift, the UNICEF Headquarters Micronutrient Unit has become the Child Survival and Nutrition Unit, and USI and fortification have moved to the Growth and Development Unit, both Units remaining in the Nutrition section (UNICEF 2005).

The basic assumptions of the thesis were that:
1. There are a common set of necessary factors that are common to successful programmes, and
2. Conversely, there are factors and situations, which if not in-place, make success less likely.

The **hypothesis** was stated as:
that the first set of international micronutrient goals was not reached globally because identifiable steps and pre-conditions were not met.

The earlier chapters have described the characteristics of the main vitamins and minerals of public health interest, the impact of deficiencies of these micronutrients and the programmes used to address these deficiencies and their impact on health, growth, neuro-intellectual development and national development. It then went on to look at the policy aspects; the adoption by the multilateral agencies and the global health and nutrition community in committing politically to eliminating or reducing micronutrient (vitamin and mineral) deficiencies through a series of international goals, most recently those of the UN Special Session on Children in 2002 and less directly the Millennium

Development Goals. Progress towards these goals and attempts to identify what makes an effective and successful programme, and increasingly in recent times, a sustainable one, has attracted a great deal of attention and funding over the last few decades. Micronutrient interventions have become accepted policy interventions. While these have been primarily vertical programmes, in recent years micronutrient interventions have become integral parts of other programmes, such as vitamin A with the National Immunization Days of the polio eradication programme, vitamin A with measles immunization, iron and various B vitamins to fortify flour and condiments, multimicronutrients for use in emergencies and HIV endemic populations, and so on. USI (universal salt iodization) has not been directly involved in such integrated programmes although there is on-going efficacy, and effectiveness, research into double fortification with iron (Diosady & Mannar 2000), and even triple with vitamin A (Zimmermann 2004b), and the testing of household salt samples during Child Health Weeks. The increasing attention to zinc and folic acid and to multimicronutrient supplementation has seen an increasing number of recommendations, funding and programmes directed towards these, although some contentious points remain, but all will likely expand as programmes (unless some of the current research shows unexpected findings) (Christian et al. 2005, Huffman, Habicht, Scrimshaw 2005, Shrimpton et al. 2005, SCN/WHO/UNICEF 2006).

Taking all that has gone before, what can be concluded? This will be considered broadly by looking at: progress, constraints to achieving the goals; facilitating factors; and finally, an assessment of the likelihood of achieving the current goals (one has already passed the due date of end of 2005) by 2010 (and in the broader context of the Millennium Development Goals) by 2015.

8.2 Progress

There is no doubt there has been enormous progress, particularly, as seen in chapter 5, over the last two decades. This progress has been measured at various points and is relatively consistent. Even during the global downturn in progress to reduce undernutrition in the 1990s (ACC/SCN 1997, SCN 2004), micronutrient programming continued to grow for reasons discussed in Chapter 4.

8.2.1 Vitamin A deficiency and its disorders (VADD):

Reduction in global vitamin A deficiency has shown considerable progress, and has probably been under-estimated because few countries have sequential data, and the estimation of vitamin A deficiency is relatively difficult. This difficulty of assessing the magnitude of the problem accurately has lead to very wide variations in estimates from 125 million to 250 million (West 2002), and there is currently no universally endorsed figure, although WHO is working on an updated estimate. How to assess the likely impact of vitamin A supplementation at the national level is being addressed at present, especially given the promised reduction of child mortality in advocacy to Governments. So far, this has been based on presumed reductions of the numbers based on the meta-analyses that were done showing a likely 23% decline with at least 70% coverage with 2 doses of VAC annually (Beaton et al. 1993, West & Darnton-Hill 2000). However, it is understood that not always the same children are receiving the capsule twice a year, and that expected outcomes, and impact, depend on region and previous prevalence, and that monitoring often is imprecise. Consequently figures have often been projected as 'lives saved', which is useful for donors' requirements but unlikely to be very accurate. It has recently been noted that emphasis by donors on 'lives saved' figures by different interventions is exceeding the number of children actually dying. This will ultimately cause a loss of credibility to Governments, International Agencies and Civil Society partners and donors. The CHERG project in WHO is currently working with UNICEF and other partners to agree on some figures and the methods behind them (Wardlaw, personal communication 2005).

A further factor, since the goals were established, is that it is clear that many women, up to 15% in countries such as Nepal (Christian 2002), are also vitamin A deficient and this shows up as night-blindness during pregnancy- common enough in some societies to be considered a 'normal' part of pregnancy. These numbers have not generally been included but have been estimated to be nearly 20 million women in the developing world having low vitamin A- slightly fewer than one third of these being clinically night blind (West 2002). Consequently progress has been measured by coverage of vitamin A capsules in (generally) children 6 months to 6 years, but even this has been misleading as UNICEF used for a time the 'coverage with at least 1 capsule over the last year', which would not give adequate protection to a child. This is in the process of being changed to ensuring two doses each year with the indicator being 'a vitamin A capsule

within the last six months' (Dalmiya et al. 2005). Progress over the last 15 years has been from only 16% of children in targeted countries protected by the requisite two doses per year in the 1990s to over half (52%) in 2003 (Dalmiya et al. 2005) as seen in chapter 5, and this progress is continuing with the success of Child Health Weeks and the scaling-up of other Child Survival and Development integrated interventions. These estimates do not include food-based projects that in some localities, e.g. parts of rural Bangladesh, may have had considerable impact at the household level (Talukder et al. 2000, HKI 2003). Currently, sustainability is not being measured in any agreed-to way, and will become an issue as currently there is only one main donor (CIDA), with support in a limited number of countries by USAID. Nevertheless, small but increasing numbers of countries are now buying their own supplements (Dalmiya, Palmer, Darnton-Hill 2006).

8.2.2 Iodine Deficiency disorders (IDD):

Iodine deficiency has been classified as eliminated in 72 countries, and great progress made in most other affected countries with another 40 with only mild iodine deficiency (WHO 2004, UNICEF 2006). Almost 70% of affected households now have iodized salt (UNICEF PFC 2006). This measure (household coverage with adequately iodized salt), along with urinary iodine and another ten process indicators (now consolidated into seven) are being monitored (WHO/UNICEF/ICCIDD 2001) as seen in chapter 5. The data show impressive progress. As the data are looked into more closely it is clear that one of the ways forward, besides ensuring sustainability, is to concentrate on the quality of the iodization, as some large countries with good levels of coverage often have short falls in quality e.g. India. Using iodization of salt as an indicator of likely progress to sustained elimination of iodine deficiency, in the early 1990s coverage of households was estimated to be about 20%. By the mid-decade it was upto to 50% and by 2001, 70%. There is some suggestion it then plateaued, or even declined to 67-68% but that was probably largely an artifact as new, and probably more challenging, countries were being assessed and providing data, and there was improved accuracy of assessments, but not entirely. Although the UN goal was not reached (and was unreasonably optimistic in the first place) there has been increased activity by bodies such as UNICEF, ICCIDD and the Network for the Sustainable Elimination of IDD, and the USI coverage picked up over the last couple of years, and the latest figure is 69% (UNICEF 2006). It

was anticipated that the figure will be higher after analysis in 2006 of the MICS and DHS survey data. In fact it has turned out to be not much changed because of new countries and several large population countries not improving their coverage- however, many more countries showed marked improvement. Nevertheless, the UN Goal of elimination was not reached by the end of 2005, but this does not negate the enormous progress that has been made.

UNICEF, WHO, ICCIDD, the Network for Sustained Elimination of IDD, MI and GAIN, with AusAID, CIDA and USAID, are making plans for an urgent last push in the face of funding declines e.g. by the Kiwanis and the Gates Foundation. There will also be increased attention to ensuring sustainability in those countries with good coverage, as well as those taking their coverage levels from below 90% and increasing it. So, even though the actual goal was not reached, on-going plans have been developed and a major assessment is being prepared that will include the findings from the presumed improved current rounds of new data on household coverage by iodized salt. The remaining countries have been divided into 16 'make-or-break' countries- large countries in which success would mean a global coverage of over 85%, other countries that are almost there and need a final push, and countries that need to achieve sustainability (Untoro, personal communication 2007). The Gates Foundation has expressed interest in helping to support finishing this 'unfinished agenda'.

8.2.3 Iron deficiency and anaemia:

Programmes addressing iron deficiency and anaemia have been the least successful for a variety of reasons. Even the fortification programmes going on for many years in the Americas may have been less useful (especially in Latin America) because of the type of fortificant used. One review of progress in this area (Mason et al. 2004) found there were so few countries with good monitoring, or even repeated surveys at national level, that the authors could make no comment on the likely progress. Nevertheless, they concluded, as have most others, that there has been little progress, even though most countries have national policies mandating iron and folic acid for pregnant women (Darnton-Hill, Paragas, Cavalli-Sforza 2007). The logistics are poor, especially in countries with poorly resourced and functioning health systems, and compliance not much better. Consequently levels of anaemia, especially in pregnant women remain

high, especially in South Asia and sub-Saharan Africa. Global data have just been released by WHO, showing little change in prevalence (with comments on inappropriateness of comparison because of methodological differences), and showing the big regional disparities which demonstrate the global inequity aspect of this deficiency (McLean et al. 2007). Anaemia prevalence remains around 40-60% in women of Africa and South Asia and 50-65% in children; in terms of the contribution to the global burden of disease, it ranks 9th of all global diseases (Stoltzfus 2003, Stoltzfus, Mullany, Black 2004). It has been estimated that the number of iron/folic acid supplements being supplied by UNICEF, even in countries that are unlikely to be sourcing them elsewhere, is grossly less than the estimated number required. The evidence for the impact of iron (and usually B vitamins) fortification of wheat, and less often maize, flour is surprisingly poor, but the low prevalences of anaemia seen in more affluent countries is generally attributed to the long-standing practice of fortification with iron and B vitamins (MI/UNICEF 2003, Bishai & Nalubola 2002).

A possible constraining issue for infant and young child prevention and control of iron deficiency anaemia through supplementation is the final outcome and consensus following a major trial in Pemba, Tanzania. That study showed higher mortality and hospitalization in undernourished children in a malaria-endemic area who were given iron supplementation (Sazawal et al 2006). Nevertheless, a smaller sub-study also showed that children treated with anti-malarials, anthelminthics and iron had the best outcomes. There also remains some scepticism about the importance of iron deficiency to intellectual development by some. Immediately after the paper was published in the Lancet, WHO called a small expert consultation to examine the findings and make recommendations on supplementation. However this was extremely contentious and the recommendations rather too vague for use in the field and there are an ongoing series of activities planned to operationalize the conclusions and recommendations.

Consequently, there is currently considerable interest in looking at new interventions and approaches. These include fortification of different vehicles such as soy sauce in China and fish sauce in Vietnam, using different fortificants such as FeEDTA, and continued work on bio-fortification to produce higher yielding plant crops with less phytate and more iron and zinc. However, this last is likely to be a long-term intervention in terms of impact and consequently home-based fortification is seen as a more likely avenue for

reducing anaemia in infants and young children- through the use of encapsulated iron and other micronutrients as 'sprinkles', or crushable tablets that can be added to complementary foods. Different delivery mechanisms, such as to adolescents, so they go into their first pregnancy with adequate stores has been proven to be efficacious and in some settings at least, effective (Cavalli-Sforza et al. 2005). Weekly or bi-weekly doses may also improve compliance and lower costs and have been shown to have a similar impact (Schultink et al. 1996, Gross et al. 1997, Viteri et al. 1997) and is likely to be recommended by WHO after a recent Global Expert Consultation in the Western Pacific Regional Office.

8.2.4 Other micronutrients:

The data on other micronutrients are even poorer. The two micronutrients that have come to the public attention in the last decade mostly are folate and zinc, although other vitamins have their lobbies, such as vitamin B12, riboflavin, thiamin, and selenium. The data on folate are relatively poor, and often judged by referral to levels of neural tube defects, although this is likely to be also influenced by socio-economic factors, and the prevalence of genetic polymorphisms in different ethnic populations (Stover & Garza 2002). It is unlikely that much progress has been made except where it has happened by increased affluence or fortification. China appears to have had a successful programme of giving folic acid supplementation pre-pregnancy, but this is thought not likely to be effective in many other cultural settings. In the countries of the South East Asia and the Western Pacific WHO Regions, operational research has been on-going (Cavalli-Sforza et al. 2005) in the weekly supplementation of folic acid and iron, including in adolescents, with promising results. In affluent countries, folic acid supplementation has not been very successful, nor have attempts to increase the intake of folate-rich foods, in the younger and lower socioeconomic status women- precisely those to whom the programmes were addressed. Fortification of flour has been shown to be effective in reducing neural tube defects in national programmes in Canada and the USA (MI/UNICEF 2003), and is being introduced into Australia and the UK, and this seems likely to become the norm, including in Europe, at least in countries consuming adequate wheat, or other flours, to make a difference if fortified (Abramsky & Dolk 2007). It seems likely that low vitamin B12 levels are also a risk factor for neural tube defects in newborns, apart from concerns about masking vitamin B12 deficiency, so for both these

reasons, vitamin B12 should probably also be added to the fortification mix, especially in countries like India (Ray et al. 2007). A recent meta-analysis confirmed also an impact in stroke prevention, which will no doubt encourage its adoption (Wang et al. 2007).

Zinc suffers from the difficulty of its measurement, so even the estimates of the size of the global deficiency problem are very unsure and based on apparent consumption. Nevertheless, intervention studies showing the impact on infectious disease and decreases in mortality from diarrhoeal and respiratory diseases do suggest it is a widespread problem especially in poverty-stricken countries. The evidence showing a reduction in severity and incidence of diarrhoea is sufficiently strong that there is now a WHO/UNICEF recommendation on the use of zinc for two weeks in cases of diarrhoea, along with ORT (WHO/UNICEF 2004). There is a lot of activity, especially from the group IZiNCG and briefly, the Gates Foundation-funded Zinc Taskforce, to examine the need for zinc to also be seen as a micronutrient with preventive properties, both against diarrhoea and lower respiratory tract infections (Hotz and Brown 2004). How to get the zinc to infants and children, especially in resource poor settings, is a challenge but another vertical programme seems unlikely to be funded and so should be done with other micronutrients e.g. 'sprinkles'. A recent meeting in Vienna examined indicators and prevalence (de Benoist et al. 2007) and WHO plans to have an Expert Consultation in mid-2008 to make recommendations on scaling-up activities, as the Child Survival approach would suggest (Jones et al. 2003).

It is likely that other micronutrient deficiencies have declined in prevalence in affluent countries, and especially the more affluent parts of these populations. In countries such as the USA, something like 70% of pregnant women take multimicronutrient supplements during pregnancy and many others routinely take them on a daily basis. However, in low-income countries, multiple micronutrient deficiencies are still relatively common (Huffman et al. 1998, Mason et al. 2005, MI/UNICEF 2003), as might be expected with poor quality diets and higher disease burdens. Because of the difficulty in establishing the size of the problem, and the relatively little public health attention being paid to them, it has more or less been presumed that as diets and socio-economic conditions improve, the intakes of these other micronutrients will also be improved. However, judging on the prevailing prevalences of undernutrition, for most poor populations, especially in sub-Saharan Africa and South East Asia, this improvement is

not happening anything like equally, even in countries where average rates of undernutrition have shown improvement (SCN 2004, UNICEF 2006). Consequently, multi-micronutrient approaches are being increasingly adopted as e.g. with fortification, and in multimicronutrient supplementation of pregnant women and adolescents, and in children and women in emergencies.

In last two years, two guidance notes or recommendations have been endorsed. Firstly, in response to a study in Tanzania with multiple micronutrients, using a somewhat idiosyncratic formulation but which showed a positive response in terms of reducing HIV progression and symptoms of AIDS (Fawzi et al. 2004), there was a meeting and a review of the literature commissioned, to give the background for the recommendation for HIV+ pregnant women to receive one supplement daily of multiple micronutrients at the level of one RDA (UNICEF/WHO/UNU 1999). The other was the WHO/UNICEF/WFP recommendation of a vitamin and mineral supplementation to infants and young children, and to pregnant and lactating women, in emergencies, at the appropriate RDA level (WHO/UNICEF/WFP 2005). Further meetings are planned to examine, and make policy, on a series of efficacy and effectiveness studies on multimicronutrient supplementation and low birth weight.

8.3 Achieving the goals: constraints and facilitating factors

Both constraints and facilitating factors were summarized in chapter 6, using the UNICEF Nutrition framework under four broad areas: basic or global (mega-) factors; underlying or national (macro-) factors; underlying or sub national (meso-) factors; and, proximal or immediate community and household factors (micro-) (Figure 6.1) (UNICEF 1998), and by matrices (Table 6.1). In essence the main factors included:

- demonstrated commitment by government and a relevant policy in place
- a knowledge of the magnitude of the problem
- an awareness of the public health and social consequences by all levels
- an intersectoral approach
- an awareness of the direct link to poverty, socio-economic and politico-social issues, and hence the need to address these specifically, as part of micronutrient deficiencies prevention and control programmes
- initial presence of external funding
- a ‘champion’ both internationally and nationally

In the view of the writer, much more attention has been paid to the most proximal events rather than those underlying and distal, although this approach might be seen as having a limited sustainability and hence on-going impact. This is because little in the environment that caused the deficiencies in the first place is really being changed; such things as poverty, social and political disadvantage and inequities (UNDP 2003, 2005, Fogel 2004), and accessibility to staples such as rice (Torlesse, Kiess, Bloem 2003). The Bellagio Study Group on Child Survival Lancet papers specifically noted that they were only focusing 'on proximal causes of death and on selected environmental and behavioural risk factors' (Black, Morris, Bryce 2003), and interventions that are mainly done through health systems, many of which are dysfunctional and under-resourced in the countries with the highest burden of disease and micronutrient deficiencies (Millennium Project 2005).

However, there is a new awareness that inequities increased in the 1990s due to inappropriate (at least for the poor) global trade and other policies, as well as poor governance in many countries and heavy indebtedness (Lancet 1993, SCN 1997). The role of some of these constraints in health are now at least recognized (Sachs 2001). The new maternal, neonatal and child survival initiatives should have an impact at the proximal level (PMNCH 2005). Much depends on the wealthier countries committing, and supplying the resources, to achieving the MDGs, as they have promised, but the funds are proving slow to come in (UNDP 2003, 2005). It is likely fairer trading practices would have an even greater impact than many more proximal interventions (Chopra & Sanders 2004, Chopra & Darnton-Hill 2006). However, the Doha round of WTO talks, essentially trying to reduce industrialized countries subsidies on commodities including food (Stevens & Kennan 2001), is having considerable progressing. Many would argue that the next rounds on services could also negatively impact on health and education systems in the poorest countries, already suffering from poor infrastructure- a direct result of 'structural adjustment' (Lancet 1993) amongst other things, and a massive brain drain from low income countries (UN Millennium Project 2005), and inadequate research funding on diseases of the developing world (WHO 2005b). The World Bank itself has recently published an annual report (2006) showing that the poorer countries, and especially the very poor of most countries, have not benefited from globalization whereas the majority of countries have.

Clearly, in improving micronutrient status in poor populations, as in other health and nutrition interventions, there needs to be special attention to the poorest populations in affected countries. Recent debt forgiveness in 17 of the poorest 18 countries should help (Financial Times 2005), especially if used wisely to invest in improved health and education infrastructure and human resources (UN Millennium Project 2005) and does not result in other promised resources being replaced or delayed. It is also encouraging that donors such as CIDA and DFID are again willing to invest in human resources in these countries. The Lancet Child survival articles have demonstrated the disproportionate burden on the 42 poorest countries of the world (Black, Morris, Bryce 2003). The new Partnership for Maternal, Neonatal and Child Health is specifically targetting the 60 highest child mortality countries. From a child rights perspective, all children need to be protected from micronutrient and other nutrient deficiencies wherever they are. If the various goals can be achieved, even in the poorest countries, then undernutrition in the widest sense will have been addressed. However the trajectory in many countries is not encouraging (World Bank 2005, UNICEF 2004, UNICEF 2006).

8.4 Achieving the goals: will that happen?

The question is easy to answer for the goals of the 1990 World Summit for Children goals and the FAO/WHO ICN 1992 goals that were to be achieved by 2000- the end of the decade goals. Although, as has been seen, much progress was made in addressing vitamin A deficiency and IDD prevention and control, the actual goals of elimination were not achieved. Little progress was made in iron. The overall lack of achieving the goals provoked remarkably little comment, which suggests that there was not really an expectation that this achievement would happen, and that they were indeed generally regarded as a goal rather than an anticipated outcome. This resulted in some discussion (see e.g. Arthur 2001, SCN 2001) as to whether goals are useful or not, how donor driven they are, and whether it was a useful exercise or not. Many argued that the progress that had been made, and the attention and resources paid to micronutrient deficiencies would not have happened without there being specific goals to aim for (and for donors to have as ‘goal posts’).

Whatever conclusion may or may not have been drawn, there was intensive activity in drawing up new UN goals prior to the Special Session of the UN General Assembly in

2002 (UNICEF 2001). It was not conceivable that any group involved in the different aspects of international health would have risked not having a UN Goal, however sceptical they might have been. The micronutrient goal was expanded in 2001 to include iron deficiency and other anaemias for infants and children, included other micronutrients, and specified intervention forms of fortification, supplementation and food-based approaches. As noted, the Millennium Development Goals do not include explicit micronutrient goals, but achieving them will not be possible without addressing micronutrient deficiencies and undernutrition (SCN 2004), and indeed, unless nutrition-directed activities are not further mainstreamed into the development of low-income countries (Veneman 2005), as recently persuasively advocated by the World Bank (World Bank 2006b).

The question is now will these most recent goals be reached? So, disaggregated by micronutrient, the current WFFC goals (UNICEF 2002) are predicted as follows.

8.4.1 To achieve sustainable elimination of iodine deficiency disorders by 2005

The iodine deficiency disorders are addressed first as this goal was due to be reached at the end of 2005. As noted, enormous progress has been made, both in identifying the magnitude of the problem and in the coverage of iodized salt, which is currently almost 70% (UNICEF 2006) and is expected to be higher as the latest MICS and DHS data are analyzed. UNICEF and partners have developed a strategy aimed at reaching the goal by prioritizing countries according to five categories (Mangasaryan et al. 2005). Firstly, those with the largest number of unprotected foetuses are targetted. These are generally related to size of the population e.g. China with >90% coverage and therefore by definition, having eliminated the problem, still has over one million unprotected foetuses being born each year, especially in the most socio-economic vulnerable areas. Secondly there are the countries that have achieved good coverage and just need an extra push; thirdly, those that are salt-exporting countries and that would have a major impact on countries to which they export, many of which import all their salt. Then there are the countries who have eliminated the problem but who need to ensure sustainability of this; and finally, emergency situations, and countries which will not achieve USI for a variety of other reasons, including heavy reliance on small salt producers.

These countries will therefore require other approaches as well as salt iodization, such as supplementation (both oral and rarely, intramuscular, with iodized oil) (Untoro et al. 2007) or even iodization of water supplies and condiments, although alternative approaches to USI continue to remain controversial inside UNICEF. WHO held an Expert Consultation in 2005 on revised guidelines for supplementation, and there was a follow-up meeting with UNICEF in New York later in the year to look implementation aspects (WHO in press, Untoro et al. 2007). This effort is now being joined by other partners under the aegis of an over-arching strategy. The current scorecard is that approximately 70% of at-risk households have access to iodized salt, and iodine nutrition is optimal or above in 72 countries (5 with apparently excessive intakes), but still moderately to severely inadequate in 14 and no data from 66 countries (WHO 2004, Andersson et al. 2005).

IDD has a spotted history of sustainability even in countries that are affluent e.g. Australia, Germany, the Netherlands, that have had successful coverage of iodized salt in the past, including most of the previous Soviet countries, and countries with internal strife have seen their previously high coverage drop (Andersson et al. 2005, Andersson et al. in press). Although in many countries this has been addressed in the current decade and the last one, the possibility of complacency and back-sliding will always remain. To a certain extent, the easier targets have been reached and it is the remaining 10-30% of the population not yet reached globally that will be a bigger challenge and will be less cost-effective to address.

The goal was not achieved but very impressive progress made towards elimination has been made, and while funding is not going to be as it was, plans for sustainability are increasingly being endorsed by countries. As noted, the Bill & Melinda Gates Foundation are currently negotiating with UNICEF and GAIN to ensure funding over the next five years to complete 'the unfinished agenda' and aims to ensure sustainability. Nevertheless it will be important to continue with global advocacy for some years to come. Besides a major review at the end of next year, there is likely to be one in 2010, along with the other micronutrients.

8.4.2 To achieve sustainable elimination of vitamin A deficiency by 2010

Vitamin A has also made impressive progress especially with xerophthalmia, which is now relatively rare globally. Some of this progress was thought to be unlikely to be maintained as high coverage by vitamin A supplementation in many of the poorest countries was through linkages with the national Polio Immunization Days, but strategies such as those being identified by countries with UNICEF, MI/CIDA, A2Z/USAID, and others, to develop a post-NIDs strategy are leading to some optimism. Recent experience with Child Health Days/Weeks and incorporation in Child Survival and Development packages has demonstrated that routine and/or 'pulse' approaches can achieve coverage over 70% and higher (Dalmiya 2007). However, the capsules are still being bought by CIDA funds in many cases, so sustainability is less clear. There will need to be increasing effort on sustainability for vitamin A interventions, including getting purchase of capsules into national health budgets. Twenty-seven countries now have a national budget line or have included vitamin A supplements in 'basket funding' through the World Bank sector-wide approaches (SWAps) and other mechanisms (Dalmiya et al. 2005, UNICEF 2007). This will help sustainability (it is often pointed out that Bangladesh has had a vitamin A supplementation policy for over 30 years). A further vitamin A global strategy is currently being developed by UNICEF, MI, USAID and other partners (Dalmiya et al. 2006).

Whether the actual goal of global sustainable elimination will be reached will depend on the integration into national programmes of maternal, neonatal and child survival approaches, where it is increasingly treated as a health commodity, much like an immunization, rather than as part of the nutrition input. Whether this is finally helpful towards achieving the goal in a sustainable way, as vitamin A supplementation becomes increasingly part of Child Survival type activities, coverage is expected to increase. Already coverage with two supplements per year has increased from 16 countries in 1999 to 72 in 2005 (of the 103 countries affected) (UNICEF 2007). Encouragingly, it is the highest risk regions showing greatest success e.g. East Asia & Pacific at 82%, Sub-Saharan Africa 73%, and South Asia 71% of eligible children receiving two doses (UNICEF 2007).

8.4.3 To reduce by one third the prevalence of anaemia, including iron deficiency, by 2010

As consistently noted, there has been little progress using current methods. So, while the goal will almost certainly not be reached, new approaches are likely to increase coverage. Iron deficiency and other anaemias, will be partially addressed by increased spread of effective methods of fortification with iron, folic acid and other B vitamins (and sometimes vitamin A and zinc). The emphasis has been on widely consumed cereal and staple crops, but condiments appear to be having early success e.g. soy sauce in China and fish sauce in Vietnam. There will be increasing application of newer formulations such as multimicronutrients, new approaches such as weekly or bi-weekly dosing, addressing adolescents, and fortification, including home fortification such as the 'sprinkles' approach. As Stoltzfus (2003) has noted, the 'question is not only one of sustainability [of current supplementation programmes], because at this point there is little or no success to be sustained.' She also notes that in industrialized countries it is being controlled by mostly private sector actions, iron-rich foods through animal-based and fortified foods diet, and by iron-fortified weaning foods.

8.4.4 To accelerate progress towards reduction of other micronutrient deficiencies, through dietary diversification, food fortification and supplementation [presumably also by 2010].

Other micronutrient deficiencies are very likely to be reduced, especially through increased fortification, increased policy recommendations and increased use of multimicronutrient supplements. However, some possible questions of safety have been raised on supplementation of pregnant women in Asia (Christian et al. 2005) although these non-significant effects have been vigorously questioned (Huffman, Habicht, Scrimshaw 2005, Shrimpton et al. 2005). Supplementation with multiple micronutrients is now a recommendation for HIV+ women, and for infants, young children and pregnant and lactating women in emergencies (WHO/WFP/UNICEF 2006). The extent of usage in HIV endemic populations is still being debated, although in resource-poor settings, these are often the only alternative when anti-retroviral therapy is unavailable, and so have become widely used anyway. The appropriate formulations and dosages will be an important area of investigation in the coming years. The availability of supplements in

infants and young children, including in HIV-endemic populations, and especially in emergency situations, will also be accelerated, although, especially in the former population, some questions remain about the safety of iron and zinc (although is likely to be more a matter of appropriate dosing).

Nevertheless, this is an area likely to accelerate in the child survival and development approaches, as well as widespread increased availability of fortified complementary foods, including with folic acid and zinc, and possibly vitamin B12, extension of zinc probably as part of multimicronutrient supplementation and fortification into prevention of diarrhoea and respiratory diseases, as well as treatment of diarrhoea, and increased use of multimicronutrients in acute and chronic emergencies. The possible impact of 'bio-fortification' remains to be seen (Darnton-Hill, Margetts, Deckelbaum 2004) but could be considerable (Bouis 2002), especially if potential crops such as 'golden rice' live up to some of the projected claims for it. Other food-based approaches, if adopted on a widespread basis e.g. orange-flesh sweet potato, high beta-carotene-containing bananas, and cereals modified to be high micronutrient-containing by breeding or by being genetically modified, may all have an impact if widely adopted. Fortification, beyond staples, is also likely to play a larger role e.g. bouillon cubes made by the private sector and fortified in West Africa, and oils in many countries.

Dietary diversification as an intervention continues to be bedevilled by poor funding and unreasonable scepticism. However, as evidence continues to accumulate, such activities will continue to go forward, often through NGO activity, and maybe given a boost by any successes with 'bio-fortification'. The role of genetic manipulation remains to be seen, but is not thought to have a great impact on nutritional status, and certainly not until as much effort is put into nutritional aspects as in crop yields, and only if there is wider acceptance of the technology (Darnton-Hill, Margetts, Deckelbaum 2004). Increased information on the demonstrated effects of female education and empowerment of women and the resulting increased income being spent preferentially on children's health and education will also be seen as a positive input into poverty alleviation programmes, and hence part of nutrition programmes (Smith & Haddad 2003).

Nevertheless, in terms of the current decade goal, the part of the goal for 'other micronutrient deficiencies' is very likely to be reached, especially through increased

fortification, increased policy recommendations and increased use of multimicronutrient supplements.

8.5 The future for micronutrient deficiency prevention and control

The stated contention that the original (1990-2000) goals were not reached for identifiable reasons is largely supported, although it seems clear that national and local factors also played different roles in different settings. Firstly, micronutrient interventions were often not integrated at the community and district level e.g. vitamin A capsules and immunization were very infrequently integrated, except for the relatively short-lived National Polio Immunization Days, including having separate reporting systems and being implemented by different sections of the Health Ministry. Secondly, the micronutrient programmes, including universal salt iodization (USI), were often seen as externally driven e.g. by donors, or in the case of USI as a 'UNICEF Programme'. As part of this, the goals were sometimes seen as an external, international goal, not necessarily as relevant to the perceived or documented needs of the country, despite virtually all countries having signed off on them. Thirdly, clearly ineffectual programmes continued to be promoted e.g. iron/folic acid supplementation. It has never been clear why folic acid would be given to pregnant women when it is often started well into the second trimester, after the protective potential has passed; or to infants and young children particularly those in malaria-endemic areas when they are receiving anti-folate antagonist anti-malarials. While iron supplementation is efficacious, it seems rarely effective in resource-poor settings. While this has been known for a long time, it has rarely been acted upon. Iron supplementation programmes has been unnecessarily 'medicalized'- certainly the international scientific 'iron community' have been strikingly unable to come up with, or endorse, innovative delivery solutions e.g. weekly or bi-weekly, appropriate fortification vehicles and so on (Darnton-Hill, Paragas, Cavalli-Sforza 2007). The current controversy over iron supplementation to infants and young children is likely to have repercussions beyond malaria-endemic areas. Fourthly, inadequate health and other systems with poor infrastructure and inadequate staffing have made delivery of many health interventions, including micronutrient supplementation, difficult. Finally, in the face of continuing and often increasing social disparities and other inequities, diets will not improve and neither will delivery systems.

The biggest reason for the goals not being reached of course, is the likelihood that they were excessively optimistic. No other disease, except smallpox, has been eradicated, or even eliminated by conscious human effort, and so it is unclear why a recurring problem like a deficiency of vitamins and minerals would be, without a massive change in social conditions for those most likely to have insufficient dietary intakes. The eradication of poliomyelitis, with far greater resources, and more physiological logic, remains incomplete. The chances of success with micronutrient elimination and reductions would seem to be particularly problematic during a time when levels of undernutrition are either getting worse in some countries, or where the rate of improvement was slowing down in others (SCN 2004, UNICEF 2006).

There is a large degree of consensus that the micronutrient deficiencies prevention and control as a global initiative has been largely donor-driven. This is not, in itself, a criticism as the negative impacts on health and development are real and so the need for policies, programmes and resources are increasingly being accepted by the countries themselves. This has been bolstered by a considerable degree of success in addressing micronutrient malnutrition up to now. Nevertheless if the efforts remain predominantly donor-driven, it does not argue well for sustainability. As has been pointed by Oomen 30 years ago, Europe eliminated vitamin A deficiency without a specific programme over a century ago through improved social conditions, economic growth and improved nutrition, including the fortification of margarine with vitamins A and D (Oomen 1976).

The success of future directions will depend on three things: (i) continuity of donor support; (ii) the degree to which countries buy-in to micronutrients as a priority- often in the face of such other imperatives as also dealing with the HIV and malaria pandemics, including the rising tide of obesity and noncommunicable diseases in disadvantaged populations (Yach, Kellogg, Voute 2005, Garrett & Ruel 2005); and, (iii) political and socio-economic fortunes of countries (currently mainly those peri-Equatorial countries with a high levels of poverty) (UNDP 2003). Currently, none of these look particularly promising.

Continuity of donor funding is essential in the short-term as are continuing efforts to reduce global inequities and accelerate progress in the achievement of the MDGs. Possibilities that might improve the picture are that some countries will have undoubtedly

improved socio-economically e.g. India, and are increasingly managing their own programmes, including funding. If now greater equity can be achieved, as seems likely with the increased emphasis on poverty reduction and improved health and education access schemes, this will be a major help in addressing the problem. However progress on the child survival (MDG4), and that on eradicating hunger (MDG1) are not encouraging, without increased acceleration. However, there are some encouraging signs at all four policy and implementation levels: (i) globally, with increased aid and the debt cancellation of 17 of the most highly indebted countries and the adoption of new global recommendations on multimicronutrient supplementation and fortification, and the vastly increased emphasis on maternal, neonatal and child survival programmes; (ii) nationally, with signs of increased adoption of fortification and national ownership of some programmes; (iii) at the district level, adoption of integrated, known and evidence-based interventions for child survival and development; and, (iv) locally, an increase in education for girls in many countries. The beauty of micronutrient interventions are that they can be moving ahead while the global community continues to struggle to get its act together in so many ways. Sustainability of successes in reducing vitamin and mineral deficiencies remains the outstanding question.

References

Abramsky L, Dolk H on behalf of the EUROCAT Folic Acid Working Group. Should Europe fortify a staple food with folic acid? Lancet. 2007;369:641-2.

ACC/SCN. Policies to improve nutrition: What was done in the '80s. (JMB/SRG). UN Administrative Coordinating Committee/Standing Committee on Nutrition. SCN News 1990;6:7-20.

ACC/SCN. First Report on the World Nutrition Situation. United Nations Administrative Committee on Coordination/Subcommittee on Nutrition. Geneva:ACC/SCN. 1987.

ACC/SCN. Second report on the World nutrition situation. Administrative Coordinating Committee's subcommittee on nutrition. Geneva: World Health Organization. 1992;1.

ACC/SCN. Meeting the Nutrition Challenge: a call to arms. Statement made by the SCN at its 24th Session, 25th March 1997, Kathmandu, Nepal. 1997a. http://www.unsystem.org/SCN/archives/scnnews14/ch05.htm (accessed June 23, 2007).

ACC/SCN. Third Report on the World Nutrition Situation. Geneva: United Nations Administrative Committee on Coordination/Subcommittee on Nutrition. 1997b.

ACC/SCN. Adequate Food: A Human Right. Administrative Coordinating Committee, Subcommittee on Nutrition. Symposium hosted by UNHCHR, Geneva, Switzerland. SCN News. 1999:18.

ACC/SCN. The Fourth Report on the World Nutrition Situation. Nutrition through the life cycle. United Nations Administrative Committee on Coordination/Subcommittee on Nutrition, in collaboration with the International Food Policy Research Institute. Geneva:ACC/SCN. 2000.

ACC/SCN. Nutrition goals and targets. Administrative Coordinating Committee, Subcommittee on Nutrition. Geneva: World Health Organization. 2001;22:5-31.

Agte VV, Chiplonkar SA, Tarwadi KV. Factors influencing zinc status of apparently healthy Indians. J Amer Coll Nutr. 2005;24:334-41.

Aguayo VM, Baker SK. Vitamin A deficiency and child survival in sub-Saharan Africa: a reappraisal of challenges and opportunities. Food Nutr Bull. 2005;26:348-55.

Aguayo VM, Baker SK, Crespin X, Hamani H, MamadoulTaïbou A. Maintaining high vitamin A supplementation coverage in children: lessons from Niger. Food Nutr Bull. 2005;26:26-31.

Aguayo VM, Bégin F, Boy E, Codling K, Darnton-Hill I, Gorstein J, Greig A, van Ameringen M, Fryars M. Life beyond NIDs? Harnessing regular health services to protect all children against vitamin A deficiency. Presented at an ancillary special session, IVACG, Lima, Peru. October 2004. UNICEF/MI. Report in Preparation.

Ahmed F, Hassan N, Kabir Y. Vitamin A deficiency among adolescent female garment factory workers in Bangladesh. Eur J Clin Nutr. 1997;51:698-702.

Ahmed F, Khan MR, Faruque MO, Taj S, Hyderi T, Jackson AA. Serum retinol is influenced by social factors and antioxidant nutrient among adolescent girls in urban Bangladesh. Int J Food Sci Nutr. 1998;49:39-44.

Ahmed F. Vitamin A deficiency in Bangladesh: a review and recommendations for improvement. Publ Health Nutr. 1999;2:1-14.

Ahmed F, Darnton-Hill I. Vitamin A. In: Gibney MJ, Margetts B, Kearney JM, Arab L (eds.). Public Health Nutrition. The Nutrition Society Textbook Series. Oxford: Blackwell Sciences Ltd. 2004;chp11:192-215.

Åke Persson L, Eneroth HH, Ekström E-C. Multiple micronutrient supplementation during pregnancy. A review of effects on birth size, maternal haemoglobin, and perinatal mortality demonstrated in trials in Bangladesh, Guinea-Bissau and Pakistan. Report prepared for UNICEF. International Maternal and Child Health, Uppsala University, Sweden. Unpublished. 2004.

Akhter N. Household and community level determinants of malnutrition in Bangladesh. Nutrition Surveillance Project Bulletin No.17. Helen Keller International/Institute of Public Health Nutrition. HKI Bulletin 2006;17:1-4.

Alderman H, Horton S. The economics of addressing nutritional anaemia. In: Kraemer K, Zimmermann M (eds.). Nutritional anaemia. Basel:Sight & Life Press. 2007;chp3:19-35.

Allen LH. How important is dietary quality for the growth and development of children in developing countries? Food Nutr Bull. 1991;63:15-8.

Allen LH. Ending hidden hunger: the history of micronutrient deficiency control. Background paper for the World Bank/UNICEF Assessment Study. Washington,DC:World Bank. Unpublished paper. 2000.

Allen LH, Ahluwahlia N. Improving iron status through diet: The application of knowledge concerning dietary iron availability in human populations. OMNI/USAID. Arlington,VA: JSI. 1997.

Allen LH, Gillespie S. What works? A review of the efficacy and effectivenesss of nutrition interventions. UN ACC/SCN/ADB. ACC/SCN Nutr Policy paper no.19/ADB Nutr Devel Ser no.5. Manila: Asian Development Bank. 2001.

Allen LH, Jones KM. Vitamin B-12. In: Coates P (ed.). Encyclopedia of Dietary Supplements. New York: Marcel Dekker. 2005.

Alnwick DJ. Combating micronutrient deficiencies: problems and perspectives. Proc Nutr Soc. 1998a;75:1-12.

Alnwick DJ. Weekly iodine supplements work. Am J Clin Nutr. 1998b;67:1103-4.

Andersson M, Takkouche B, Egli I, Allen HE, de Benoist B. Current global iodine status and progress over the last decade towards the elimination of iodine deficiency. Bull Wld Hlth Org. 2005;83:518-25.

Andersson M, de Benoist B, Darnton-Hill I, Delange F. Iodine deficiency in Europe: a continuing public health problem. WHO/NHD. Geneva: World Health Organization. In press.

Arab L, Gibney M, Margetts B, Kearney JM (eds). Public Health Nutrition. The Nutrition Society Textbook series. Oxford: Blackwell Science. 2004;chp11:192-215.

Arthur P. De-emphasize nutrition goals and targets in nutrition work: now. Administrative Coordinating Committee, Subcommittee on Nutrition. SCN News. Geneva: World Health Organization. 2001;22:5.

Arthur P, Kirkwood B, Ross D, Morris S, Gyapong J, Tomkins A, Addy H. Impact of vitamin A supplementation on childhood morbidity in northern Ghana. Lancet. 1992;339:361-2.

Ash DM, Latham MC, Tatala SR, Mehansho H, Ndossi N, Frongillo EA jr. Trial of a micronutrient fortified beverage supplement in school children and pregnant women in Tanzania. In: XIXth IVACG Report 'Vitamin A and other micronutrients: biologic interactions and integrated interventions'. Washington, DC:IVACG/USAID/ILSI Research Foundation. 1999; Abstracts 23:90.

Balls A. IMF approves debt relief for poorest countries. Financial Times 2005 December 22;2. Available from: http://news.ft.com/cms/s/48388ce4-7279-11da-9ff7-0000779e2340.html (accessed 22 December 2005).

Baltussen R, Knai C, Sharan M. Cost-effectiveness analysis of iron fortification and iron supplementation to reduce iron deficiency in four sub-regions of the world. J Nutr 2004;134:2678-84.

Barclay AJG, Foster A, Sommer A. Vitamin A supplements and mortality related to measles: a randomised clinical trial. Br Med J. 1987;294:294-6.

BASF. The fortification of staple foods with vitamin A. Human Nutrition: flour fortification. Undated:2pp. www.food.fortification.com (accessed 16 February 2005)

BASICS. (Acharya K, Sanghvi T, Diene S, Stapleton V, Seumo E, Srikantiah S, Aminu F, Ly C, Dossou V). Using the 'Essential Nutrition Actions (ENA)' to accelerate coverage with nutrition interventions in high mortality settings. Washington,DC:BASICS II. 2004.

Bauerfeind JC (ed.). Vitamin A deficiency and its control. London: Academic Press. 1986.

Beard JL. Iron biology in immune function, muscle metabolism and neuronal functioning. J Nutr. 2001;131:568 -80S.

Beard JL, Stoltzfus RJ (eds.). Iron-deficiency anemia: reexamining the nature and magnitude of the public health problem. 2001;131;no.2S-II: 564S-703S.

Beaton GH, Martorell R, Aronson KJ, Edmonston B, McCabe G, Ross AC, Harvey B. Effectiveness of vitamin A supplementation in the control of young child morbidity and mortality in developing countries. ACC/SCN State of the Art Series Nutrition Policy Discussion Paper, No. 13. Geneva: Administrative Committee on Coordination/Sub-Committee on Nutrition (ACC/SCN). 1993.

Beaton G, McCabe G. Efficacy of intermittent iron supplementation in the control of iron deficiency anaemia in developing countries. An analysis of experience. Final report to the Micronutrient Initiative. Ottawa:MI. 1998.

Begin F, Greig A. Food Fortification in West Africa: assessment of opportunities and strategies. A background paper prepared for "A public-private sector dialogue on food fortification in West Africa", Ghana. Ottawa:The Micronutrient Initiative. 2002.

Behrman JR, Rozenweig MR. The returns to increasing body weight. Penn Institute for Economic Research. Philadelphia: University of Pennsylvania. 2001;PIER Working paper 01:052:41pp.

Behrman JR, Alderman, Hoddinott J. Hunger and malnutrition. Copenhagen Consensus Challenge Paper. Copenhagen Consensus. 2004:58pp. Available from: www.copenhagenconsensus.org

Bellagio Study Group on Child Survival. Knowledge into action for child survival. Lancet. 2003;362:323-7.

Bender D. Daily doses of multivitamin tablets. Br Med J. 2002;325:173-4.

Bengoa JM, Rueda-Williamson R. Planning and organization of a national food and nutrition policy. In: Beaton GH, Bengoa JM (eds.). Nutrition in Preventive Medicine. WHO Monogr Ser No.92. Geneva:World Health Organization. 1976:419-44.

Berwick DM. Lessons from developing nations on improving health care. Br Med J. 2004;328:1121-9.

Bhargava A, Jukes M, Lambo J, Kihamia CM, Lorri W, Nokes C, Drake L, Bundy D. Anthelmintic treatment improves the hemoglobin and serum ferritin concentration of Tanzanian schoolchildren. Food Nutr Bull. 2003;24:332-42.

Bicego GT, Boerma JT. Maternal education and child survival: a comparative study of survey data from 17 countries. Soc Sci Med. 1993;36(9):1207-27.

Bishai D, Nalubola R. The history of food fortification in the United States: its relevance for current fortification efforts in developing countries. Econ Development Cultural Change. 2002;51(1):37-53.

Black RE. Zinc Deficiency, infectious disease and mortality in the Developing World. J Nutr. 2003;133:1485S-9S.

Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? Lancet. 2003;361:2226-34.

Blankhart DM. Individual intake of food in young children in relation to malnutrition and nightblindness. Trop Geogr Med. 1967;19:144-53.

Blaxter K. People, food and resources. Cambridge: Cambridge University Press. 1986.

Bleichrodt N, Garcia I, Rubio C, Morreale de Escobar G, Escobar Del Rey F. Development disorders associated with severe iodine deficiency. In: Hetzel BS, Dunn JT, Stanbury JB (eds.). The prevention and control of iodine disorders. Amsterdam: Elsevier. 1987:65-84.

Bleichrodt N, Born M. A meta-analysis of research on iodine and its relationship to cognitive development in iodine-deficient children. In: Stanbury J (ed.). The damaged brain of iodine deficiency. New York: Cognizant Communication Corporation. 1994:195-200.

Block SA, Kiess P, Kosen S, Moench-Pfanner R, Bloem MW, Timmer CP. Did Indonesia's crisis of 1997/98 affect child nutrition? A cohort decomposition analysis of national nutrition surveillance data. Tufts Nutrition discussion paper No.5. Food Policy and Applied Nutrition program. Tufts University. http://wwwnutrition.tufts.edu/publications/fpan (accessed 17 March 2004).

Bloem MW. Interdependence of vitamin A and iron: An important association for programmes of anaemia control. Proc Nutr Soc. 1995;54:501-8.

Bloem MW. Post-modernism and nutrition. In: Semba RD, Bloem MW (eds.). Nutrition and Health in Developing Countries. 2nd ed. Totowa, NJ: Humana Press. In press.

Bloem MW, Wedel M, Egger RJ, Speek AJ, Chusilp K, Saowakontha S, Schreurs WH. A prevalence study of vitamin A deficiency and xerophthalmia in Northeastern Thailand. Am J Epedimiol. 1989;129:1095-1103.

Bloem MW, Wedel M, Agtmaal EJ, van Speek AJ, Saowakontha S, Schreurs WHP. Vitamin A intervention: Short-term effects of a single, oral, massive dose of vitamin A on iron metabolism. Am J Clin Nutr. 1990;51:76-9.

Bloem MW, Huq N, Gorstein J, Burger S, Khan T, Islam N, Baker S, Davidson F. Production of fruits and vegetables at the homestead is an important source of vitamin A among women in rural Bangladesh. Eur J Clin Nutr.1996;50:S62-S7.

Bloem MW, de Pee S, Darnton-Hill I. Vitamin A deficiency in India, Bangladesh and Nepal. Malnutrition in South Asia. A regional profile. UNICEF Regional Office for South Asia. 1997:125-1444.

Bloem MW, de Pee S, Darnton-Hill I. New issues in developing effective approaches for the prevention and control of vitamin A deficiency. Food Nutr Bull.1998;19:137-48.

Bloem MW, de Pee S, Graciano F, Kiess L, Moench-Pfanner R, Talukder A. Homestead food production- A strategy to combat malnutrition and poverty. Jakarta, Indonesia: Helen Keller International/Asia-Pacific. 2001a.

Bloem MW, Darnton-Hill I. Micronutrient deficiencies: first link in the chain of nutritional and health events in economic crises. In: Bendich A, Deckelbaum RJ (eds.). Primary and Secondary Preventive Nutrition. Volume 2. Totowa, NJ:Humana Press. 2001b;357-74.

Bloem MW, de Pee S, Darnton-Hill I. Micronutrient deficiencies and maternal thinness: First chain in the sequence of nutritional and health events in economic crises. In: Bendich A, Deckelbaum RJ (eds.). Preventive Nutrition: The comprehensive guide for health professionals. 3rd ed. Totowa, NJ: Humana Press. 2005:chp27:689-710.

Bohr O, Darnton-Hill I. Millennium development goals and micronutrients. Internal UNICEF paper. 2003.

Bouis HE. A new tool for fighting micronutrient malnutrition. Symposium: Plant breeding: A new tool for fighting micronutrient malnutrition. Special issue. J Nutr. 2002a;132: 3 491S-4S.

Bouis HE. Three criteria for establishing the usefulness of biotechnologyfor reducing micronutrient malnutrition. Food Nutr Bull. 2002b;23:351-3.

Bouis HE. Micronutrient fortification of plants through plant breeding: can it improve nutrition in man at low cost? Proc Nutr Soc. 2003;62:403-11.

Bouis HE, Lineback D, Scheeman B. Bio-technology–derived nutritious foods for Developing Countries: needs, opportunities, and barriers. Food Nutr Bull. 2002;23:342-83.

Bourdoux P, Mafuta A, Hanson A, Ermans AM. Cassava toxicity: the role of linamarin. In: Ermans A (ed.). Role of cassava in the etiology of endemic goitre and cretinism. Canada: International Development Research Centre (IDRC). 1980:15-27.

Boyages SC, Collins JK, Maberly GF, Jupp FJ, Morris JG, Eastman CJ. Iodine deficiency impairs intellectual and neuromotor development in apparently normal people: a study of rural inhabitants from North Central China. Med J Aust. 1989;150:676-82.

Brabin BJ, Hakimi M, Pelletier D. An analysis of anemia and pregnancy-related maternal mortality. J Nutr. 2001;131:604S-15S.

Brent RL, Oakley GP. The folate debate. Pediatr. 2006;117:1418-9.

Brown LR. Outgrowing the Earth: the food security challenge in an age of falling water tables and rising temperatures. Earth Policy Institute. New York:WW Norton& Co. 2005:177-94.

Brown KH, Black RE, Nahar S, Sawyer J. Consumption of foods and nutrients by weanlings in rural Bangladesh. Am J Clin Nutr. 1982;36:878-89.

Brown KH, Wuehler SE (eds.). Zinc and human health. Ottawa:Micronutrient Initiative. 2000.

Bryce J, el Arifeen S, Pariyo G, Lanata CF, Gwatkin D, Habicht J-P, & the multi-country evaluation of IMCI study group. Reducing child mortality: can public health deliver? Lancet. 2003;362:159-64.

Bryce J, Black RE, Bhutta ZA, Lawn JE, Steketee RW. Can the world afford to save the lives of 6 million children each year? Lancet. 2005;365:2193-200.

Brundtland GH. Address to the Fifty-fifth World Health Assembly.Geneva, World Health Organization, 13 May, 2003. Unpublished.

Bürgi H. Iodine deficiency disorders in Switzerland. In: Delange F, Robertson A, McLoughney E, Gerasimov G (eds.). Elimination of Iodine Deficiency Disorders (IDD) in Central and Eastern Europe, the Commonwealth of Independent States, and the Baltic States. WHO/EURO/NUT/98.1. Geneva: World Health Organization. 1998:15-19.

Buse K, Walt G. Global public-private partnerships. Part II: what are the health issues for global governance? Bull Wld Health Org 2000;78:699-709.

Bushamuka VN, de Pee S, Talukder A, Keiss L, Panagides D, Taher A, Bloem MW. Impact of a homestead gardening program on household food security and empowerment of women in Bangldesh. Food Nutr Bull. 2005;26:17-25.

Caballero B. Global patterns of child health: The role of nutrition. Ann Nutr Metab. 2002;46 Suppl1:3-7

Callens K, Phiri E. Household food security and nutrition in the Luapula Valley, Zambia. Food Nutr Agriculture. 1998;22:22-9.

Calloway DH. Human nutrition: food and micronutrient relationships. Agricultural strategies for micronutrients. IFPRI Working paper 1. Washington,DC: International Food Policy Research Institute. 1995.

Carneiro I, Roca-Feltrer A, Schellenberg JA. Estimating the burden of malarial anaemia in children under five years in sub-Saharan Africa. Roll Back Malaria/WHO. Geneva: World Health Organization. 2006. http://www.lshtm.ac.uk/dcvbu/staff/aroca_feltrer.htm (accessed June 22, 2007).

Carnoy M. The case for investing in basic education. New York: UNICEF. 1992

Caulfield LE, Black RE. Zinc deficiency. In: Ezzati M, Lopez AD, Rodgers A, Murray CJL. (eds.). Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Vol 1. Geneva: World Health Organization. 2004; 5:257-80.

Caulfield LE, de Onis M, Blössner M, Black RE. Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles. Am J Clin Nutr. 2004;80:193-8.

Cavalli-Sforza LT. Community mobilization and social marketing to prevent anaemia with weekly iron/folic acid supplements in women of reproductive age in Cambodia, The Philippines and

Vietnam. Presented at UNICEF EAPRO Workshop on 'The use of micronutrients to enhance foetal and infant growth: a review of effectiveness trials'. Bangkok, Thailand. June 2004.

Cavalli-Sforza LT, Xu W, Wu K, Lu F, Liu Q, Siri E, Ferro-Luzzi A. Anaemia, rickets and protein-energy malnutrition during the weaning period in a rural community of the People's Republic of China. Unpublished paper. 1991:1-7.

Cavalli-Sforza LT, Rosnan A, de Boer AS, Darnton-Hill I. Nutritional aspects of changes in disease patterns in the Western Pacific Region. Bull Wrld Hlth Org. 1996;74:307-18.

Cavalli-Sforza LT, Berger J, Smitasiri S, Viteri F. Summary: weekly iron-folic acid supplementation of women of reproductive age: impact overview, lessons learned, expansion plans and considerations towards achievement of the Millennium Development Goals. Nutr Rev. 2005;63(II):S152-8.

Cervinskas J, Houston R. Monitoring vitamin A programs. Ottawa: The Micronutrient Initiative. 1998.

Chavasit V, Nopburabutr P, Kongkachuichai R. Combating iodine and iron deficiencies through the double fortification of fish sauce, mixed fish sauce, and salt brine. Food Nutr Bull. 2003;24:200-7.

Child Health Research Project. Zinc for Child Health. Black R (ed.). Child Health Research Project Special Report. Baltimore, MD: Johns Hopkins School of Public Health. 1997;(1):3-17.

Chopra M. Risk factors for undernutrition of young children in a rural area of South Africa. Publ Hlth Nutr. 2003;6(7):645-52.

Chopra M, Galbraith S, Darnton-Hill I. A global response to a global problem: the epidemic of overnutrition. Bull Wld Hlth Org 2002;80:952-8.

Chopra M, Sanders D. Child health and poverty. London:Childhood Poverty Research and Policy Centre, Save the Children. 2004;CHIP Report No.10:1-61.

Chopra M, Darnton-Hill I. Responding to the crisis in Sub-Saharan Africa: the role of nutrition. Publ Hlth Nutr. 2006;9:544-50.

Christian P. Recommendations for indicators: Night blindness during pregnancy- a simple tool to assess vitamin A deficiency in a population. J Nutr. 2002;132:2884S-8S.

Christian P. Micronutrients and reproductive health issues: an international perspective. J Nutr. 2003;133:1969S-73S.

Christian P, West KP Jr., Khatry SK, et al. Night blindness of pregnancy in rural Nepal - nutritional and health risks. Int J Epidemiol. 1998a;27:231-37.

Christian P, West KP Jr., Khatry SK, et al. Vitamin A or β-carotene supplementation reduces but does not eliminate maternal night blindness in Nepal. J Nutr. 1998b;128:1458-63.

Christian P, West KP Jr, Khatry SK, Kimbrough-Pradhan E, LeClerq SC, Katz J, Shrestha SR, Dali SM, Sommer A. Night blindness during pregnancy and subsequent mortality among women in Nepal: Effects of vitamin A and β-carotene supplementation. Am J Epidemiol. 2000;152:542-7.

Christian P, West KP Jr, Khatry SK, Leclerq SC, Pradham EK, Katz J, Shrestra SR, Sommer A. Effects of maternal micronutrient supplementation on fetal loss and infant mortality: a cluster-randomized trial in Nepal. Am J Clin Nutr. 2003;78:1194-1202.

Christian P, Osrin A, Manandhar DS, Khatry SK, Costello AM, West K. Antenatal micronutrient supplements in Nepal. Letter. Lancet. 2005;366:711-2.

Cobra C, Muhilal, Rusmil K, Rustama D, Djatnika, Suwardi SS, Permaesih, D, Muherdiyantiningsih, Martuti S, Semba RD. Infant survival is improved by oral iodine supplementation. J Nutr. 1997;127:574-8.

Codling K, Dalmiya N, Darnton-Hill I, de Pee S, Shrimpton R, Sunawang S, Zagré NM, Huffman SL. Programmatic implications of multimicronutrient supplementation effectiveness trials in pregnancy in Developing Countries. Food Nutr Bull. In press.

Cohen N, Jalil MA, Rahman H, Matin MA, Sprague J, Islam J, Davison J, Leemhuis de Regt E, Mitra M. Landholding, wealth and risk of blinding malnutrition in rural Bangladeshi households. Soc.Sci.Med. 1985;21:1269-72.

Cohen N, Rahman H, Sprague J, Jalil MA, Leemhuis de Regt E, Mitra M. Prevalence and determinants of nutritional blindness in Bangladeshi children. Wld Health Stat Quart. 1985;38:317-30.

Copenhagen Consensus. How to spend $50 million to make the World a better place. 2004. www.copenhagenconsensus.com (accessed October 6, 2006).

Copenhagen Consensus. Today's challenge- tomorrow's opportunity. 2004. http://www.copenhagenconsensus.com/Default.aspx (accessed December 27, 2005).

Cousoudis A, Pillay L, Spooner E, Kuhn L. Coovadia HM. Randomized trial testing the effect of vitamin A supplementation on pregnancy outcomes and early mother-to-child HIV-1 transmission in Durban, South Africa. South African Vitamin A Study Group. AIDS 1999;13:1517-24.

Coutsoudis A, Pillay K, Spooner E, Kuhn L, Coovadia HM and for the South African Vitamin A Study Group. Influence of infant-feeding patterns on early mother-to-child transmission of HIV-1 in Durban, South Africa: a prospective cohort study. Lancet. 1999;354:471-6.

Crop Biotech Update. IRRI and CIMMYT to work on 4 research priorities. Global Knowledge Center on Crop Biotechnology, International Service for the Acquisition of Agri-Tech Applications SEAsiaCenter (ISAAA), AgBiotechNet. January, 2005:1-2.

Csete J. Importance of understanding the aetiology of anaemia. Research in Action. New York:UNICEF. 1997:7.

Cutter J, Tan BY, Chew SK. Levels of cardiovascular disease risk factors in Singapore following a national intervention programme. Bull Wld Hlth Org 2001;79:908-15.

Dalmiya N, Darnton-Hill I, de Benoist B, Andersson M. The role of UNICEF and WHO in eliminating iodine deficiency disorders. In: Hetzel B, Delange F, Dunn JT, Ling J, Mannar V, Pandav C (eds.). Towards the global elimination of brain damage due to iodine deficiency. Delhi: Oxford University Press. 2004; 5:52-72.

Dalmiya N, Palmer A, Greig A, Darnton-Hill I. Vitamin A supplementation: progress for child survival. New York:UNICEF. Partnership for Maternal, Neonatal and Child Survival. Countdown Conference. London School of Hygiene and Tropical Medicine. London, UK. December, 2005.

Dalmiya N, Palmer A, Darnton-Hill I. Sustaining vitamin A supplementation requires a new vision. Lancet. 2006;doi:10.1016/S0140-6736(06)69336-7:12-14.

Dalmiya N, Palmer A, Greig A. Vitamin A supplementation: a decade of progress. Working paper. New York:UNICEF. 2006.

Dalmiya N. Results from the Child Health Day assessments. Preliminary findings: Ethiopia, Tanzania and Uganda. Presented at the Global Immunization Meeting at the UN, New York. 13-15 February 2007 (article in preparation).

Darmon N, Ferguson EL, Briend A. A cost constraint alone has adverse effects on food selection and nutrient density: an analysis of human diets by linear programming. J Nutr. 2002;132:3764-71.

Darnton-Hill I. Vitamin A deficiency in Bangladesh. Health Policy & Planning. 1988a;3:205-13.

Darnton-Hill I. Vitamin A fortification of wheat: Bangladesh experience. Presentation at the Regional Vitamin A Meeting. Latest Advances in the Control of Vitamin A Deficiency and Its Impact on Health. Jakarta, Indonesia: Indonesian Ministry of Health/WHO,SEARO/HKI. 1988b.

Darnton-Hill I. Vitamin A deficiency in Bangladesh: prevention and control. Dhaka:Helen Keller International. 1989a.

Darnton-Hill I. Vitamin A fortification of wheat: Bangladesh experience. In: Latest Advances in the Control of Vitamin A Deficiency and Its Impact on Health. Report of a Regional Workshop. Jakarta: Government of Indonesia/WHO,SEARO/HKI. 1989b:121-35

Darnton-Hill I. Vitamin A in the Third World. Proc Nutr Soc Aust. 1989c;14:13-23.

Darnton-Hill I. Report of a WHO consultancy to Mongolia. Manila: Western Pacific Regional Office of the World Health Organization. 1995.

Darnton-Hill I. Developing industrial-governmental-academic partnerships to address micronutrient malnutrition. Nutr Rev. 1997;55:76-81.

Darnton-Hill I. Control and prevention of micronutrient malnutrition. Asia Pac J Clin Nutr. 1998a;7:2-7.

Darnton-Hill I. Overview: rationale and elements of a successful food fortification program. Food Nutr Bull. 1998b;19:92-100.

Darnton-Hill I. Solving the micronutrient problem in the Asia Pacific Region. Asia Pac J Clin Nutr. 1998c;7:245-5.

Darnton-Hill I. The challenge to eliminate micronutrient malnutrition. Aust NZ J Publ Hlth. 1999a;23:307-14.

Darnton-Hill I. Micronutrient intervention programmes in countries of the Western Pacific Region of WHO- the role of NGOs. Presented at the Working Group on accelerating progress in controlling micronutrient malnutrition. Kuala Lumpur, Malaysia. Western Pacific Regional Office of the World Health Organization/Institute of Medical Research. 1999b.

Darnton-Hill I. Partnerships in eliminating malnutrition. SCN News: United Nations system's forum for nutrition. Advisory Committee on Corrdination/ Subcommittee on Nutrition (ACC/SCN). 1999c;19:2.

Darnton-Hill I. Multiple Approaches and Partnerships in Public Health Nutrition interventions. Nutrition. 2000;16:633-6.

Darnton-Hill I, Hassan N, Karim R, Duthie M. Tables of Nutrient Composition of Bangladeshi Foods: English version with particular emphasis on vitamin A content. Dhaka: HKI/INFS/WFP. 1988.

Darnton-Hill I, Sibanda F, Mitra M, Ali MM, Drexler AE, Rahman MH, Samad Khan MA. Distribution of vitamin-A capsules for the prevention and control of vitamin-A deficiency in Bangladesh. Food Nutr Bull. 1988;10:60-70.

Darnton-Hill I, Truswell AS. Thiamin status of a sample of homeless men in Sydney, Australia. Med J Aust. l990;152:5-9.

Darnton-Hill I, Charrondiere UR, Volmanen PVE, Nair NVK. Food and nutrition policy development in the Western Pacific Region of WHO. Proc 6th Asian Congress on Nutrition (ACN). 1991:361-5.

Darnton-Hill I, Cavalli-Sforza LT, Volmanen PVE. Clinical nutrition in East Asia and the Pacific. Asia Pac J Clin Nutr. 1992;1:27-36.

Darnton-Hill I, Sriskandarajah N, Stewart PM, Craig G, Truswell AS. Vitamin supplementation and nutritional status in homeless men. Aust J Publ Hlth. 1993;17:246-51.

Darnton-Hill I, Volmanen PVK, Tai M. Recent experience with a regional strategy: elimination of iodine deficiency disorders in the Western Pacific Region of WHO. In: Nutrition in a Sustainable Environment. London:Smith-Gordon. 1994:283-6.

Darnton-Hill I, Canova K, Bolasny D, Houston R, Kohler R, Ferris-Morris M, Rajabiun S, Sanghvi T, Weinstein H, Wilbur S. The OMNI experience: using global lessons to move local programs. Final report of the fully-USAID funded Opportunities for Micronutrient Interventions Project 1993-1998. Arlington, VA: John Snow Inc. 1998a:1-79.

Darnton-Hill I, Coyne ET. Feast and famine: socioeconomic disparities in global nutrition and health. Publ Hlth Nutr. 1998b;1:23-31.

Darnton-Hill I, Nishida C, de Boer A, Volmanen P, Cavalli-Sforza LT. Food and nutrition policy development. Asia Pac J Clin Nutr. 1998c;7:103-10.

Darnton-Hill I, Mora JO, Weinstein H, Wilbur S, Nalubola PR. Iron and folate fortification in the Americas to prevent and control micronutrient malnutrition: an analysis. Nutr Rev. 1999;57:25-31.

Darnton-Hill I, Bloem MW, de Benoist B, Brown L. Micronutrient restoration and fortification: communicating change, benefits and risk. Asia Pac J Clin Nutr. 2000;11(S6):S184-S196.

Darnton-Hill I, Nalubola R. Food fortification as a public health strategy to meet micronutrient needs- successes and failures. Proc Nutr Soc. 2002;61:231-41.

Darnton-Hill I, Margetts BM, Deckelbaum R. Public health nutrition and genetics: implications for nutrition policy and promotion. Proc Nutr Soc. 2004;63:173-85.

Darnton-Hill I, Webb P, Harvey PWJ, Hunt JM, Dalmiya N, Chopra M, Ball MJ, Bloem MW, de Benoist B. Micronutrient deficiencies and gender: social and economic costs. Am J Clin Nutr. 2005a;819:1198S-205S.

Darnton-Hill I, Margetts BM, Chopra M, Nishida C, Bloem MW. Globalization, economics and nutrition: where are we going? Proceedings of the 18th International Congress of Nutrition. Nutrition Safari for Innovative Solutions. Vorster HH, Blaauw R, Dhansay MA, Kuzwayo PMN, Moeng L, Wentzel-Viljoen E. (eds.). Basel: Karger. Ann Nutr Metab. 2005b:5.

Darnton-Hill I, Bloem MW, Chopra M. Achieving the Millennium Development Goals through mainstreaming nutrition: speaking with one voice. Publ Hlth Nutr. 2006;9:537-9.

Darnton-Hill I, Kennedy E, Hossain SMM, Cogill B. Solutions to nutrition-related health problems of preschool children: education and nutritional policies for children. J Pediatr Gastroenterol Nutr. 2006;43:S54-S65.

Darnton-Hilll I, Chopra M. International Nutrition: a double burden for public health. In: Lawrence M, Worseley A (eds.). Public Health Nutrition: from principles to practice. Sydney:Allen & Unwin. 2006;10:223-46.

Darnton-Hill I, Paragas N, Cavalli-Sforza LT. Global perspectives: accelerating progress on preventing and controlling nutritional anaemia. In: Kraemer K, Zimmermann MB (eds.). Nutritional anaemia. Basel: Sight & Life/DSM. 2007:21:359-82.

Dary O. Free Trade vs Public Health: the history of the fighting for the sugar fortification program in Guatemala. In: XXth IVACG Report '25 Years of progress in controlling vitamin A deficiency: looking to the future'. Vietnam, Feb 12-15 2001. Washington DC: IVACG/USAID/ILSI Research Foundation. 2001 Abstracts. W5:59.

Dary O, Freire W, Kim S. Iron compounds for food fortification: Guidelines for Latin America and the Caribbean. Nutr Rev. 2002;60(7):S50-S61.

Dary O, Mora J. Food fortification to reduce vitamin A deficiency: International Vitamin A Consultative Group recommendations. J Nutr. 2002;132:2927S-33S.

Daulaire NMP, Starbuck ES, Houston RM, Church MS, Stukel TA, Pandey MR. Childhood mortality after a high dose of vitamin A in a high risk population. Br Med J. 1992;304:207-10.

de Benoist B, Martines J, Goodman T. Vitamin A supplementation and the control of vitamin A deficiency. Report of a consultation for WHO at Yverdon-les-Bains, Switzerland. Food Nutr Bull. 2001;22:213-340.

de Benoist B, Andersson M, Egli I, Takkouche B, Allen H (eds.). Iodine status worldwide: WHO global database on iodine deficiency. Geneva: World Health Organization. 2004.

de Benoist B, Darnton-Hill I, Lynch S, Allen L, Savioli L, Fontaine O. Zinc and iron supplementation trials in Nepal and Tanzania. Letter. Lancet. 2006;367:816.

de Benoist B, Davidsson L, Darnton-Hill I. The assessment of zinc status: Introduction. Food Nutr Bull. In press.

de Benoist et al. Iodine supplementation for pregnant and lactating women and infants and young children. Report of a WHO Expert Consultation. Publ Health Nutr. 2007. In press.

de Francisco A, Yasui Y, Chakraborty J. Vitamin A supplementation given to mothers after delivery reduces infant mortality and increases symptoms of morbidity. Presented at the XVI IVACG Meeting, 24-28 October, 1994, Chiang Rai, Thailand. Chiang Rai, Thailand: 1994.

de Pee S, West CE, Muhilal, Karyadi D, Hautvast JGAJ. Lack of improvement in vitamin A status with increased consumption of dark-green leafy vegetables. Lancet. 1995;346:75-81.

de Pee S, Bloem MW, Gorstein J, Sari M, Satoto, Yip R, Shrimpton R,Muhilal. Reappraisal of the role of vegetables in the vitamin A status of mothers in central Java, Indonesia. Am J Clin Nutr. 1998a;68:1068-74.

de Pee S, Bloem MW, Satoto, Yip R, Sukaton A, Tjiong R, Shrimpton R, Muhilal, Kodyat B. Impact of social marketing campaign promoting dark-green leafy vegetables and eggs in Central Java, Indonesia. Int J Vit Nutr Res. 1998b;68:389-98.

de Pee S, Bloem MW, Tjiong R, Martini E, Satoto, Gorstein J, Shrimpton R, Muhilal. Who has high vitamin A intake from plant foods, but low serum retinol concentration? Data from women in Indonesia. Eur J Clin Nutr. 1999;53:288-97.

de Pee S, Bloem MW, Kiess L. Evaluating food-based programmes for their reduction of vitamin A deficiency and its consequences. Food Nutr Bull. 2000;21:232-8.

de Pee S, Moench-Pfanner R, Martini E, Zlotkin S, Darnton-Hill I, Bloem M. Home-fortification in emergency response and transition programming: experiences in Aceh and Nias, Indonesia. Food Nutr Bull. 2007;28:189-97.

De Sole G, Belay Y, Zegeye B. Vitamin A deficiency in southern Ethopia. Am J Clin Nutr. 1987;45:780-4.

Deitchler M, Mason J, Mathys E, Winichagoon P, Tuazon MA. Lessons from successful micronutrient programs. Part I: program initiation. Food Nutr Bull. 2004a;25:5-29.

Deitchler M, Mathys E, Mason J, Winichagoon P, Tuazon MA. Lessons from successful micronutrient programs. Part II: program implementation. Food Nutr Bull. 2004b;25:30-52.

Delange F. Risks and benefits of iodine supplementation. Lancet. 1998;351:923-4.

Delange F, Iteke FB, Ermans AM (eds.). Nutritional factors involved in the goitrogenic action of cassava. International Development Research Center (IDRC):Ottawa. 1982.

Delange F, de Benoist B, Alnwick D. Risks of iodine-induced hyperthyroidism after correction of iodine deficiency disorders by iodized salt. Thyroid. 1999;6:545-56.

Delange F, Hetzel BS. The scientific basis for the elimination of brain damage due to iodine deficiency. In: Hetzel B, Delange F, Dunn JT, Ling J, Mannar V, Pandav C (eds.). Towards the global elimination of brain damage due to iodine deficiency. New Delhi: Oxford University Press. 2004;IV:151-94.

DeLong GR, Leslie PW, Wang S-H, Jiang X-M, Zhang M-L, Rakeman MA, Jiang J-Y, Ma T, Cao X-Y. Effect on infant mortality of iodination of irrigation water in a severely iodine-deficient area of China. Lancet. 1997;350:771-3.

DeMaeyer EM, Adiels-Tegman M, Raystone E. The prevalence of anaemia in the world. Wld Health Stat Quart. 1985;38:302-16.

DeMaeyer EM, Dallman P, Gurney JM, Hallberg L, Sood SK, Srikantia SG. Preventing and controlling iron deficiency anaemia through Primary Health Care, Geneva: World Health Organization. 1989.

Devadas RP. Currently available technologies in India to control vitamin A malnutrition. In: Nutr Policy Discussion paper no.2. ACC/SCN State-of-the-Art Ser. 1987:97-104.

Diosady LL, Mannar VMG. Double fortification of salt with iron and iodine. 8th World Salt Symposium Vol.2. Amsterdam:Elsevier Science BV. 2000:971-6.

Djokomoeljanto R, Tarwotjo I, Maspaitella F. Goitre control program in Indonesia. In: Ui N, Torizuka K, Nagataki S, Miyai K (eds.). Current problems in thyroid research. Amsterdam: Excerpta Medica. 1983;605:394-7.

Doherty T, Chopra M, Nkonki L, Jackson D, Greiner T. Effect of the HIV epidemic on infant feeding in South Africa: “When they see me coming with the tins they laugh at me”. Bull Wld Hlth Org. 2006;84:90-6.

Donovan A, Andrews NC. The molecular regulation of iron metabolism. Hematol J. 2004;5:373-80.

Drain PK, Kupka R, Mugusi F, Fawzi WW. Micronutrients in HIV-positive persons receiving highly active antiretroviral therapy. Am J Clin Nutr. 2007;85:333-45.

Draper A. OMNI/USAID/PCD. Child development and iron deficiency. Oxford Brief developed from a consultation held by the Opportunities for Micronutrient Interventions Project of USAID and the Partnership for Child Development. JSI. Washington,DC:ILSI Press 1997.

Dunn JT. Seven deadly sins in confronting endemic iodine deficiency, and how to avoid them. J Clin Endocrinol Metab 1996;81:1332-5.

Dyer O. UN predicts that millennium goals will be missed by a wide margin in Africa. Br Med J. 2005;330:1350.

Eastman CJ. The current status of iodine nutrition in Australia. Asia Pac J Clin Nutr. 2006(Suppl3):S67.

Edejer TT, Aikins M, Black R, Wolfson L, Hutubessy R, Evans DB. Cost effectiveness analysis of strategies for child health in developing countries. Br Med J. 2005;331:1177

El-Arifeen S, Blum LS, Hoque DME, Chowdhury EK, Khan R, Black R, Victoria CG, Bryce J. Integrated Management of Childhood Illness (IMCI) in Bangladesh: early findings from a cluster-randomized study. Lancet. 2004;364:1595-602.

Ellison JB. Intensive vitamin therapy in measles. Br Med J. 1932;2:708-11.

Englberger L, Darnton-Hill I, ET Coyne, Fitzgerald MH, Marks GC. Carotenoid-rich bananas: a potential food source for alleviating vitamin A deficiency. Food Nutr Bull. 2003;24:303-18.

Engle PL, Black MM, Behrman JR, Cabra de Mello M, Gertler PJ, Kapiriri L, Martorell R, Eming Young M, and the International Child Development Steering Group. Strategies to avoid the loss of developmental potential in more than 200 million children in the Developing World. Lancet. 2007;369:229-42.

English M, Snow RW. Iron and folic acid supplementation and malaria risk. Lancet. 2006;367:90-1.

English R, Badcock J. A community nutrition project in Vietnam: effects on child morbidity. Food Nutr Agriculture. 1998;22:15-21.

Ettyang G, Oloo A, van Marken Lichtenbelt W, Saris W. Consumption of vitamin A by breastfeeding children in rural Kenya. Food Nutr Bull. 2004;25:256-63.

Evans DB, Adam T, Tan-Torres Edejer T, Lim SS, Cassels, Evans TG, for CHOICE (WHO Millennium Development Goals Team). Time to reassess strategies for improving health in developing countries. Br Med J. 2005;331:1133-6.

Evans DB, Lim SS, Adam T, Tan-Torres Edejer T, for CHOICE (WHO Millennium Development Goals Team). Evaluation of current strategies and future priorities for improving health in developing countries. Br Med J. 2005;331:1457-61.

Ewell PT, Hagenimana V. Orange-fleshed sweetpotato as a dietary source of provitamin A: lessons from preliminary experiences in Africa. In: Abstracts of a Workshop on long-term food-based approach towards eliminating vitamin A deficiency in Africa. MRC (South Africa)/UNU/IUNS. November 2000:26.

Ezzati M, Lopez AD, Rodgers A, Van der Hoorn S, Murray CJL. Selected major risk factors and global and regional burden of disease. Lancet. 2002;360:1347-60.

Ezatti M, Lopez AD, Rodgers A, Van der Hoorn S, Murray CJL, (eds.). Comparative Quantification of Health Risks: Global and Regional Burden of Disease Attributable to Selected Major Risk Factors. Geneva: World Health Organization. 2003.

Faber M, Venter S, Benadé AJS. Increased vitamin A intake in children aged 2-5 years through targeted home-gardens in a rural South African community. Publ Hlth Nutr. 2002;5:11-6.

Fairweather-Tate SJ, Powers HJ, Minski MJ, Whitehead J, Downes R. Riboflavin deficiency and iron absorption in adult Gambian men. Ann Nutr Metab. 1992;36:34-40.

FAO. Monitoring progress since the World Food Summit. www.fao.org/monitoringprogress/index_en.html (accessed 18 February 2005).

FAO. Food fortification: technology and quality control. Report of an FAO Technical Meeting. Rome, 20-23 November 1995. FAO Food and Nutrition paper. Rome: FAO. 1996.

FAO. Assessment of the World Food Security Situation. Committee on World Food Security. 31st Session, Rome 23-26 May 2005. Rome:FAO. 2005.

FAO. Individual food intake survey methods (Ferro-Luzzi A). http://www.fao.org/docrep/005/y4249e/y4249e0a.htm (accessed June 8, 2007).

FAO/WHO. World Declaration and Global Plan of Action. International Conference on Nutrition, Rome. 1992.

FAO/WHO. Human vitamin and mineral requirements. Report of a Joint FAO/WHO Expert Consultation, Bangkok 1998. Geneva:World Health Organization. 2004.

Fawzi WW. The benefits and concerns related to vitamin A supplementation. J Infect Dis. 2006;193:756-9.

Fawzi WW, Msamanga GI, Spiegelman D, Urassa EJN, McGrath N, Mwakagile D, Antelman G, Mbise R, Herrera G, Kapiga S, Willett W, Hunter DJ, for the Tanzania Vitamin and HIV Infection Trial Team. Randomised trial of effects of vitamin supplements on pregnancy outcomes and T cell counts in HIV-1-infected women in Tanzania. Lancet. 1998;351:1477-82.

Fawzi WW, Chameres TC, Herrera MG, Mosteller F. Vitamin A supplementation and child mortality. JAMA. 1993;269:898-903.

Fawzi WW, Herrera MG, Nestel P, El Amin A, Mohammed KA. Risk factors of low dietary vitamin A intake among children in the Sudan. East Afr Med J. 1997;74:227-32.

Fawzi WW, Msamanga GI, Spiegelman D, Wei R, Kapiga S, Villamor E, Mwakagile D, Mugusi F, Hertzmark E, Essex M, Hunter DJ. A randomized trial of multivitamin supplements and HIV disease progression and mortality. New Engl J Med. 2004a;351:23-32.

Fawzi WW, Msamanga GI, Antelman G, Xu C, Hertzmark E, Spiegelman D, Hunder D, Anderson D. Effect of prenatal vitamin supplementation on lower genital levels of HIV type 1 and interleukin type 1 beta at 36 weeks of gestation. Clin Infect Dis. 2004b;38:716-22.

Fawzi WW, Msamanga GI, Urassa W, Hertzmark E, Petraro P, Willet W, Spiegelman D. Vitamins and perinatal outcomes among HIV-negative women in Tanzania. New Engl J Med. 2007;356:1423-31.

Ferrer F. *VivaLeite* program improves Brazilian children's quality of life. Nutriview. 2001;2:3.

FFI. Flour Fortification Initiative; a public-private-civic investment in each nation. 2005. http://www.sph.emory.edu/wheatflour/index.php (accessed March 25, 2007).

Fidler M, Davidsson L, Walczyk T, Hurrell R. Iron bioavailability from iron fortified fish sauce and soy sauce. In: XXth IVACG Report '25 Years of progress in controlling vitamin A deficiency: looking to the future'. Washington DC: IVACG/USAID/ILSI Research Foundation. Abstracts. 2001;F40:28.

Fiedler JL. The Nepal National Vitamin A Program: prototype to emulate or donor enclave? Heath Policy Planning. 2000;15:145-56.

Fiedler JL. The Nepal National Vitamin A Program: cost estimates for 2000 and alternative configurations of a nationwide program. Partners for Health Reform Plus. Bethesda, Maryland: Abt Associates, Inc. 2001.

Fiedler JL, Saunders M, Sanghvi T. What are the costs of interventions? Food Nutr Bull. 2007;28:S197-S203.

Field J. Multisectoral nutrition planning. A postmortem. Food Policy 1987;12:15-28.

Filteau SM, Morris SS, Abbott RA, Tomkins AM, Kirkwood BR, Arthur P, Ross DA, Gyapong JO, Raynes JG**.** Influence of morbidity on serum retinol of children in a community-based study in northern Ghana. Am.J.Clin.Nutr. 1993;58:192-97.

Finch C. Regulators of iron balance in humans. Blood. 1994;84:1697-702.

FIVIMS. An inter-agency initiative to promote information and mapping systems on food insecurity and vulnerability. http://www.fivims.net/index.jspx?lang=en (accessed 16 July 2006)

Fleck F. Rich nations should pay more to developing countries. Br Med J. 2005;330:161.

Fogel RW. Health, nutrition, and economic growth. Econ Dev Cul Change. 2004;52:643-58.

FORTAF. Fortifying Africa's future. http://www.fortaf.org/fortification_afm.htm (accessed 13 March 2007).

Frank E, Bendich A, Dennison M. Use of vitamin-mineral supplements by female physicians in the United States. Am J Clin Nutr. 2000;72:969-75.

Friis H. Micronutrient interventions and HIV infection: a review of current evidence. Trop Med Int Health. 2006;II:1849-51.

Friis H, Gomo E, Nyazema N, Ndhlovu P, Krarup H, Kaestel P, Michaelsen KF. Effect of multimicronutrient supplementation on gestational length and birth size: a randomized, placebo-controlled, double-blind effectiveness trial in Zimbabwe. Am J Clin Nutr. 2004;80:178-84.

Fusco H, Serlemitsos J. Vitamin A Fortification of Sugar in Zambia. USAID: MOST. 2001.

GAIN. Global Alliance for Improved Nutrition. Geneva:GAIN http://www.gainhealth.org/gain/ch/ (accessed October 12, 2006).

Galloway R, McGuire J. Determinants of compliance with iron supplementation: supplies, side effects, or psychology? Soc Sci Med. 1994;39:381-90.

Galloway R, Dusch E, Elder L, Achadi, Grajeda R, Hurtado E, Favin M, Kanani S, Marsaban J, Meda N, Mona Moore K, Morison L, Raina N, Rajaratnam J, Rodriquez J, Stephen C. Women's perceptions of iron deficiency and anemia prevention and control in eight developing countries. Soc Sci Med. 2002;55:529-44

Garrett JL, Ruel MT. Stunted child-overweight mother pairs: prevalence and association with economic development and urbanization. Food Nutr Bull. 2005;26:209-21.

Gerasimov G. Iodine deficiency disorders in Central and Eastern Europe, the Commonwealth of Independent States, and the Baltic States. In: Delange F, Robertson A, McLoughney E & Gerasimov G (eds). Elimination of Iodine Deficiency Disorders (IDD) in Central and Eastern Europe, the Commonwealth of Independent States, and the Baltic States. WHO/EURO/NUT/98.1. Geneva: World Health Organization. 1998:2-8.

Gerasimov G. Progress of IDD elimination through Universal salt Iodization in the Czech Republic, Slovakia, Hungary and Poland. Overview report for UNICEF Regional Office for Central and Eastern Europe, Commonwealth of Independent States and the Baltic States. Geneva:UNICEF. 2002.

Ghana VAST Study Team. Vitamin A supplementation in northern Ghana: effects on clinic attendances, hospital admissions, and child mortality. Lancet. 1993;342:7-12.

Gibney MJ, Margetts BM, Kearney JM, Arab L. Public Health Nutrition. The Nutrition Society Textbook Series. Oxford:Blackwell Science. 2004.

Gillespie S, Mason J. Controlling of vitamin A deficiency. United Nations: ACC/SCN state of the art series: Nutrition policy discussion paper no 14, 1994.

Gillespie S, Kevany J, Mason J. Controlling iron deficiency. ACC/SCN State-of-the-Art Ser Nutr Policy paper no.9. Geneva: Administrative Committee on Coordination/ Subcomittee on Nutrition. 1991.

Gittelsohn J, Shankar AV, West KP, Ram R, Dhungel C, Dahal B. Infant feeding practices reflect antecedent risk of xerophthalmia in Nepali children. Euro J Clin Nutr. 1997;51:484-90.

Glasziou PP, Mackerras DEM. Vitamin A supplementation in infectious diseases: a meta-analysis. Br Med J. 1993;306:366-70.

Godlee F. The kindness of strangers. Editorial. Br Med J. 2005;33.

Golden MH. The nature of nutritional deficiency in relation to growth failure and poverty. Acta Paediatr Scan. 1991;374:95-110.

Goodman T, Dalmiya N, de Benoist B, Schultink W. Polio as a platform: using national immunization days to deliver vitamin A supplements. Bull Wld Hlth Org. 2000;78:305-14.

Gopalan C. Child care in India- emerging challeneges. NFI Bull. Delhi:Nutrition Foundation of India. 1993;14:3.

Gorstein J, Greig A, Laviolette L, Marshall C, van Ameringen M. Life beyond NIDs? Harnessing regular health services to protect all children against vitamin A deficiency. A summary draft analysis. UNICEF/MI. Unpublished.

Grantham-McGregor S, Cheung YB, Cueto S, Glewwe P, Richter L, Strupp B and the International Child Development Steering Group. Developmental potential in the first 5 years for children in developing countries. Lancet. 2007;369:60-70.

Greger JI. Biotechnology: mobilizing dietitians to be a resource. J Am Diet Assoc. 2000;100:1306-7.

Greiner T, Mitra S. Evaluation of the impact of a food-based approach to solving vitamin A deficiency in Bangladesh. Food Nutr Bull. 1995;16:193-205.

Gross R (ed.). Micronutrient supplementation throughout the life cycle. Report of a Workshop held by the Ministry of Health, Brazil/UNICEF. New York:UNICEF. 1999.

Gross R, Dwivedi A, Solomons NW. Introduction to the proceedings of the international research on infant supplementation (IRIS) initiative. Food Nutr Bull. 2003;24:S3-S6

Gross R, Angeles-Agdeppa I, Schultink JW, Dillon D, Sastroamidjojo S. Daily versus weekly iron supplementation: programmatic and economic implication for Indonesia. Food Nutr Bull. 1997;18:64-70.

Gross R, de Romana GL, Tomaro J. A life-cycle approach to multi-micronutrients supplementation: rationale and programme concept. Food Nutr Bull. 2000;21:270-4.

Gross R, Dwivedi A, Solomons NW (guest editors). Proceedings of the International Workshop on multi-micronutrient deficiency control in the life cycle. Food Nutr Bull. 2003;24:S3-S61.

Grubesic RB. Children aged 6 to 60 months in Nepal may require a vitamin A supplement regardless of dietary intake from plant and animal sources. Food Nutr Bull. 2004;25:248-55.

Gupta P, Ray M, Dua T, Radhakrishnan G, Kumar R, Sachdev HPS. Multimicronutrient supplementation for undernourished pregnant women and the birth size of their offspring. Arch Pediatr Adolesc Med. 2007;161:58-64.

Guttikonda K, Burgess J, Hynes K, Boyages S, Byth K, Paramewaran V. Recurrent iodine deficiency in Tasmania, Australia. A salutary lesson in sustainable iodine prophylaxis and its monitoring. J Clin Endocrinol Metab. 2002;87:2809-15.

Gwatkin DR. IMCI: what can we learn from an innovation that didn't reach the poor? Bull Wld Health Org. 2006;84:768.

Haas JD, Brownlie T. Iron deficiency and reduced work capacity: a critical review of the research to determine a causal relationship. J Nutr. 2001;131;(2S-II):676S-90S.

Haddad L, Hoddinott J, Alderman H. Intrahousehold resource allocation in Developing Countries: models, methods, and policies. International Food Policy Research Institute. Washington DC: IFPRI 1997;Food Policy Statement 24.

Hagenimana V, Oyunga MA, Low J, Njoroge SM, Gichuki ST, Kabira J. The effects of women farmers' adoption of orange-fleshed sweet potatoes: raising vitamin A intake in Kenya. Washington, DC:International Center for Research on Women. ICRW/OMNI Research Rep Ser 3. 1999.

Hall A. Micronutrient supplements for children after deworming. Lancet. 2007;7:297-302.

Hallberg L, Brune M, Rossander L. Iron absorption in man: ascorbic acid and dose-dependent inhibition by phytate. Am J Clin Nutr. 1989;49:140-4.

Hallberg L, Sandstrom B, Aggett PF. Iron, zinc and other trace elements. In: Garrow JS, James WPT (eds.) Human Nutrition and Dietetics Ninth edition. Singapore: Churchill Livingstone/Longman. 1993;12:174-207.

Halsted CH. Water-soluble vitamins. In: Garrow JS, James WPT (eds.) Human Nutrition and Dietetics Ninth edition. Singapoer: Churchill Livingstone/Longman. 1993;14:239-63.

Hambidge KM, Krebs NF. Zinc deficiency: a special challenge. J Nutr. 2007;137:1101-5.

Harcourt W. The Millennium Development Goals: a missed opportunity? Development. 2005;48:1-4.

Harrison KA. Maternal mortality in anaemia in pregnancy. West Afr Med J. 1975;April:27-31.

Harrison KA, Rossiter CE. Maternal mortality. Br J Obstet Gynaecol. 1985; 92 (suppl. 5):100-15.

HarvestPlus. Breeding crops for better nutrition. http://www.harvestplus.org (accessed 15 January 2005).

Harvey PWJ, Dexter PB, Darnton-Hill I. The impact of consuming iron from non-food sources on iron status in developing countries. Publ Health Nutr. 2000;3:375-83.

Helman AD, Darnton-Hill I. Vitamin and iron status in 'new' vegetarians. Am J Clin Nutr. 1987;45:785-9.

Helwig C, Rivers J, Mason J. Micronutrient progress report 1990-2000. Trends in vitamin A deficiency, anemia, and iodine deficiency. Tulane University School of Public Health and Tropical Medicine. Draft prepared for UNICEF. 2004.

Hercberg S, Chaulica M, Galan P, Devanlay M, Zohoun I, Agboton Y, Soustre Y, Auvert B, Masse Raimbault AM, Dupin H. Prevalence of iron deficiency and iron deficiency anemia in Benin. Publ Hlth. 1988;102:73-83.

Hetzel BS. Iodine deficiency disorders: IDD and their eradication. Lancet. 1983;2:1126-9.

Hetzel BS. The story of iodine deficiency: an international challenge in nutrition. Oxford: Oxford University Press. 1989.

Hetzel BS. Iodine-deficiency disorders. In: Garrow JS, James WPT (eds.) Human Nutrition and Dietetics Ninth edition. Singapore: Churchill Livingstone/ Longman. 1993:36:534-55.

Hetzel BS. Towards the global elimination of brain damage due to iodine deficiency- the role of the International Council for Control of Iodine Deficiency Disorders. Int J Epidemiol. 2005;34:762-4.

Hetzel BS, Pandav CS. S.O.S. for a billion: the conquest of iodine deficiency disorders. 2nd ed. New York: Oxford University Press. 1996.

Hetzel BS, Delange F, Dunn JT, Ling J, Mannar V, Pandav C (eds.). Towards the global elimination of brain damage due to iodine deficiency. Delhi:Oxford University Press. 2004.

Hewett A (Executive Director, Oxfam Community Aid Abroad). Inaction speaks louder than the overblown speeches, sentiment. Sydney Morning Herald 2002 September 5. Available from: www.smh.com.au/articles/2002/09/04/1031115884378.html (accessed September 5 2002).

HKI. Monitoring the economic crisis: impact and transition, 1998-2000. Jakarta:Helen Keller International/Indonesia Nutrition and Health Surveillance System (NSS). 2000.

HKI. Evaluating national nutrition programs in Bangladesh: the role of the Nutritional Surveillance Project. Bangladesh: HKI Nutrition Bulletin. 2001a;5:1-4.

HKI. Home gardening in Hilly and Tarai areas in Nepal: impact on food production and consumption. Nepal: HKI Nutrition Bulletin. 2001b;1:1-4.

HKI. Eggs are rarely eaten in rural Bangladesh: why and how to improve their availability. HKI/IPHN Nutritional Surveillance Project Bull. No.11. Bangladesh: Helen Keller Worldwide. 2002.

HKI. Integration of animal husbandry into home gardening programs to increase vitamin A intake from foods: Bangladesh, Cambodia and Nepal. Singapore: Helen Keller International-Asia-Pacific. 2003a:1-4.

HKI. Strengthening the capacity of local NGOs through food production and nutrition programs in Bangladesh, Cambodia and Nepal. Singapore: Helen Keller International-Asia Pacific. 2003b:1-4.

HKI. Homestead food production improves household food and nutrition security. Dhaka: Helen Keller International. Homestead Food Production Bulletin. 2004 No.2:1-4.

Hoddinott J. The economic rationale for investing in nutrition. International Food Policy Research Institute. Presented at the GAIN Board Meeting. March 2007, Seattle, WA, 2007, 10pp.

Hollowell JG, Staehling NW, Hannon WH, Flanders DW, Gunter EW, Maberly GF, Braverman LE, Pino S, Miller DT, Garbe PL, DeLozier DM & Jackson RJ. Iodine nutrition in the United States: Trends and public health implications- iodine excretion data from the National Health and Nutrition Examination Surveys I and III (1971-1974 and 1988-1994). J Clin Endocrinol Metab. 1998;83 (10):3401-08.

Hossain S, Biswas R, Kabir I, Sarker S, Dibley M, Fuchs G, Mahalanabis D. Single dose vitamin A treatment in acute shigellosis in Bangladeshi children: randomised double blind controlled trial. Br Med J. 1998;316:422-6

Hotz C, Brown KH (eds.). Assessment of the risk of zinc deficiency in populations and options for its control. Food Nutr Bull. 2004;25:1-203.

Hotz C, Gibson RS. Traditional food-processing and preparation practices to enhance the bioavailability of micronutrients in plant-based diets. J Nutr. 2007;137:1097-100.

Houston R. What works? USAID-funded MOST Project. Arlington, VA:ISTI. 2001.

Houston R. Why they work: an analysis of three successful public health interventions. Vitamin A supplementation programs in Ghana, Nepal, and Zambia. Arlington,VA:ISTI. The USAID MOST Project. 2003:1-41.

Huffman SL, Baker J, Shumann J, Zehner ER. The case for promoting multiple vitamin/mineral supplements for women in underdeveloped countries. LINKAGES Project/Academy for Educational Development. Washington DC: AED/PSI. 1998.

Huffman SL, Habicht J-P, Scrimshaw N. Micronutrient supplementation in pregnancy. Lancet. 2005;366:2001.

Huffman SL, Codling K, Dalmiya N, Darnton-Hill I, Berger J, Cao Tran VH, Castillo DC, Cayad-An M, el Arifeen S, Hoque AMW, Kahn NC, de Pee S, Shrimpton R, Sunawang S, Zagré N. Programmatic implications of multiple micronutrient supplementation during pregnancy in Developing Countries. Food Nutr Bull. In preparation.

Humphrey JH, Agoestina T, Wu L, Usman A, Nurachim M, Subardja D, Hidayat S, Tielsch J, West KP Jr, Sommer A. Impact of neonatal vitamin A supplementation on infant morbidity and mortality. J Ped. 1996;128:489-96.

Humphrey JH, Rice AL. Vitamin A requirements of young infants: re-examining its need and importance. Lancet. 2000;356:422-4.

Humphrey JH, Iliff PJ, Marinda ET, Mutasa K, Moulton LH, Chidawanyika H, Ward BJ, Nathoo KJ, Malaba LC, Zijenah LS, Zvandasara P, Ntozini R, Mzengeza F, Mahomva AI, Ruff AJ, Mbizvo MT, Zunguza CD, ZVITAMBO Study Group et al. Effects of a single large dose of vitamin A, given during the postpartum period to HIV-positive women and their infants, on child HIV infection. J Infect Dis. 2006;193:860-71.

Humphrey JH, West KP, Jr., Sommer A. Vitamin A deficiency and attributable mortality among under-5-year-olds. WHO Bull. 1992;70:225-232.

Hunt JM. The potential impact of reducing global malnutrition on poverty reduction and economic development. Asia Pac J Clin Nutr. 2005;14(CD Supplement):10-38.

Hurrell RF. Preventing iron deficiency through food fortification. Nutr Rev. 1997;55:210-22.

Hurrell RF, Egli I. Optimizing the bioavailability of iron compounds for food fortification. In: Kraemer K, Zimmerman MB (eds.). Nutritional Anemia. Basel: Sight & Life Press. 2007;chp7:77-98.

Hussey GD, Klein M. A randomized, controlled trial of vitamin A in children with severe measles. N Engl J Med. 1990;323:160-4.

IAGSM (van Lerberghe W, de Brouwere V for the Inter-Agency Group for Safe Motherhood). Reducing maternal mortality in a context of poverty. 1998. http://www.itg.be/uonn/pdf/Reducing%20maternal%20mortality%20in%20a%20context%20of%2 (accessed June 23, 2007)

ICCIDD. Progress against IDD, 1998: the annual ICCIDD Board Meeting. IDD Newsletter. 1998;14:17-23.

ICCIDD. SALT 2000: Marking and sustaining Global Progress in Universal Salt Iodization. Reports from the Regions. 2000;16:1-18.

ICCIDD. From the World Health organization: current global iodine status and progress over the last decade towards the elimination of iodine deficiency. IDD newsletter 2006;22:10-12.

ICCIDD. International Council for Control of Iodine Deficiencies. http://www.people.virginia.edu/~jtd/icciddd/ (accessed 15 January 2005).

IDPAS. Iron deficiency project advisory service. International Nutrition Foundation/United Nations University/ Micronutrient Initiative. Tufts University. www.micronutrient.org/idpas/ (accesssed 4 March 2003).

IFPRI. 2020 Vision for food, agriculture and the environment. International Food Policy Research Institute. Washington, DC:IFPRI. 2000.

IFPRI. 2020 Global Food outlook. Trends, alternatives, and choices. (Rosegrant MW, Paisner MS, Meijer S, Witcover J). Washington, DC:International Food Policy Research Institute. 2001.

IFPRI (Runge CF, Senauer B, pardey PG, Rosegrant MW). Ending hunger by 2050: crucial investments and policies. Washington,DC:International Food Policy Research Institute. 2003. www.ifpri.org/ (accessed 8 March 2005).

INACG (Stoltzfus R, Dreyfus M). Guidelines for the use of iron supplements to prevent and treat iron deficiency anemia. Washington, DC: ILSI Press. 1998.

Informal Working Group on Feeding of Nonbreastfed Children. Conclusions of an informal meeting on infant and young child feeding organized by the World Health Organization. Geneva:World Health Organization. Food Nutr Bull. 2004;25:403-6.

IOM (Institute of Medicine). Prevention of micronutrient deficiencies: tools for policy makers and public health workers. Summary and key elements. Howson CP, Kennedy ET, Horwitz A (eds.). Committee on Micronutrient Deficiencies, Board of International Health, Food and Nutrition, Board of the Institute of Medicine, National Academy of Sciences. Washington, DC: National Academy Press. 1998.

IPHN/HKI. Bangladesh Nutritional Blindness survey. (Cohen N. et al.) Dhaka:Helen Keller International. 1987.

IVACG. IVACG statement on Maternal night blindness: extent and associated risk factors. Prepared by Katz J. International Vitamin A Consultative Group. Washington,DC:ILSI Research Foundation. 1996:1-5.

IVACG. Micronutrient forum: Clustering of xerophthalmia and vitamin A deficiency within communities and families. http://ivacg.ilsi.org/ (accessed March 25, 2007)

IVACG/UNICEF with MI/WHO/CIDA/USAID. Vitamin A deficiency prevention and control. International Vitamin A Consultative Group. Washington,DC:ILSI Research Foundation. 1997:1-8.

Jolly R. Early childhood development: the global challenge. Lancet. 2007;369:8-9.

Jones G, Steketee RW, Black RE, Bhutta ZA, Morris SS, and the Bellagio Child Survival Study Group. How many child deaths can we prevent this year? Lancet. 2003; 362:65-72

Jones K, Specio S, Shrestha P, Brown K, Allen, L. Nutrition knowledge and practices, and consumption of vitamin A-rich plants by rural Nepali participants and nonparticipants in a kitchen-garden program. Food Nutr Bull. 2005;26:198-208.

Jooste P, Locatelli-Rossi L. Common potholes in the salt iodization road, and how to fill them. International Council for Control of Iodine Deficiency Disorders. IDD Newsletter. 2003;19:49-51.

Jukes M, McGuire J, Method F, Sternberg R. “Nutrition and Education” In Nutrition: A foundation for Development, Geneva: ACC/SCN. 2002.

Kahaly GJ, Dietlein M. Cost estimation of thyroid disorders in Germany. Thyroid. 2002;12:909-14.

Karim R, Hassan N, Darnton-Hill I. Public policies and vitamin A intake in Bangladesh. J Nutr. 1988;1:5-12.

Katz J, Zeger SL, West KP, Jr., Tielsch JM, Sommer A. Clustering of xerophthalmia within households and villages. Int.J.Epidemiol. 1993;22:709-15.

Katz J, Khatry SK, West KP Jr, Humphrey JH, LeClerq SC, Pradhan EK, Pokhrel RP, Sommer A. Night blindness is prevalent during pregnancy and lactation in rural Nepal. J Nutr. 1995;125:2122-7.

Katz J, West KP Jr, Khatry SK, Pradhan EK, LeClerq SC, Christian P, Wu LSF, Adhikari RK, Shrestha SR, Sommer A. Low-dose vitamin A or beta-carotene supplementation has no effect on fetal loss and early infant mortality: a randomized cluster trial in Nepal. Am J Clin Nutr. 2000; 71:1570-6

Kaul S, Olson JA. Effect of vitamin A deficiency on the hydrolysis of retinoyl beta-glucuronide to retinoic acid by rat tissue organelles in vitro. Inter J Vitr Nutr Res. 1998;68:232-6.

Keith R. UNICEF: Suggestions for change. Lancet. 2005;365:292-3.

Khatry SK, West KP, Jr., Katz J, et al. Epidemiology of xerophthalmia in Nepal: a pattern of household poverty, childhood illness and mortality. Arch Ophthalmol. 1995;113:425-29.

Khush GS. Challeneges for meeting the global food and nutrient needs in the new millennium. Proc Nutr Soc. 2001;60:15-26.

Kiess L, Bloem MW, de Pee E et al. Bangladesh: Xerophthalmia free. The result of an effective vitamin A capsule program and homestead gardening (abstract) In: APHA 126th Annual Meeting Report. Washington, DC. November, 1998.

Kiess L, ur-Rashid M, Kahn T, Hye A, Darnton-Hill I, Bloem MW. Prevalence of childhood anemia and its determinants: the Bangladesh National Micronutrient Survey 1997-1998. Unpublished document. Jakarta: Helen Keller International:Asia-Pacific. 1999.

King MH, Elliott CM. Legitimate double think. Lancet. 1990;341:669-71.

Kjolhede CL, Stallings RY, Dibley MJ, Sadjimin T, Dawiesah S, Padmawati S. Serum retinol levels among preschool children in Central Java: Demographic and socioeconomic determinants. Int J Epdemiol. 1995;24:399-403.

Klemm RDW, Solon F, Fermin L, Darnton-Hill I, West KP Jr. Routine consumption of vitamin A-fortified wheat-bun did not improve growth of Filipino school children over that achieved with a non-fortified wheat-bun. Am J Clin Nutr. In press.

Kochupillai N, Pandav CS. Neonatal chemical hypothyroidism in iodine deficient environments. In: Hetzel BS, Dunn JT, Stanbury JB (eds.). The prevention and control of iodine deficiency disorders. Amsterdam:Elsevier. 1987:85-93.

Kraemer K, Zimmerman MB (eds.). Nutritional anaemia. Basel:Sight & Life/DSM. 2007.

Labonte R, Schrecker T, Sen Gupta A. A global health equity agenda for the G8 summit. Br Med J. 2005;330:533-6.

Lachapelle G. Globalization and governance: aspiring to fairer globalization. Development. 2005;48:52-60.

Lancet editorial. Structural adjustment too painful? Lancet. 1994;344:1377-8.

Lancet editorial. The world's forgotten children. Lancet. 2003;361:1.

Laviolette L. Use of fortified lozenges/candies to increase micronutrient intakes in pre-school children in India. New Delhi:Micronutrient Initiative. Personal communication. 2004.

Lawn JE, Cousens S, Zupan J for the Lancet Neonatal Survival Steering Team. 4 million neonatal deaths: When? Where? Why? Lancet. 2005;365:891-900.

Lawn JE, Costello A, Mwansambo C, Osrin D. Countdown to 2015: will the Millennium Development Goal for child survival be met? Arch Dis Child. 2007;92:551-6.

Lawrence M, Worsley T. Concepts and guiding principles. In: Lawrence M, Worsley T (eds.). Public Health Nutrition: from principles to practice. Sydney:Allen & Unwin. 2007;chp1:5-27.

Layrisse M, Chavez F, Mendez-Castellano H, et al. Early response to the effect of iron fortification in the Venezuelan population. Am J Clin Nutr. 1996;64:903-7.

Leong WI, Lonnerdal B. Hepcidin, the recently identified peptide that appears to regulate iron absorption. J Nutr. 2004;134:1-4.

Levin HM, Pollitt E, Galloway R, McGuire J. Micronutrient deficiency disorders. In: Jamison DT, Mosley WH, Measham AR, Bobadilla JL (eds.). Disease Control Priorities in Developing Countries. New York: Oxford University Press for World Bank. 1993:421-51.

Li H, Barnhart HX, Stein AD, Martorell R. Effects of early childhood supplementation on the educational achievement of women. Pediatr. 2003;112(5):1156-62.

Lindsey D, Kwaramba T. Making hammermill fortification at community level work. CARE. Nutriview. 2001;2:2.

LINKAGES. Essential health sector actions to improve maternal nutrition in Africa. Based on paper developed by the Regional Centre for Quality of Health Care at Makerere University, Uganda with LINKAGES, MOST, SARA & SANA Projects/USAID. Available from: www.RCQHC.org & www.linkagesproject.org (accessed 16 January 2005).

Lippeveld T, Orobaton N. Scaling-up key public health interventions. Information and knowledge for optimal health (INFO) Project. Arlington,VA:JSI. 2006:4.pp.

Lloyd-Puryear M, Humphrey JH, West KP jnr, Aniol K, Mahoney F, Keenum DG. Vitamin A deficiency and anemia among Micronesian children. Nutr Res. 1989;9:1007-16.

Lomborg B. How to spend $50 million to make the World a better place. New York: Cambridge University Press. 2006.

Long F, Yang Y, Wang S. Untouched land: a report on the vitamin A deficiency situation in the minority areas of Southwest China. Sight & Life Newsletter. 1998;1:28-30.

Lonnerdal B. Genetically modified plants for improved trace element nutrition. J Nutr. 2003;133:1490S-3S.

Lotfi M, Mannar MGV, Merx RJHM, Naber-van den Heuvel P. Micronutrient fortification of foods: current practices, research, and opportunities. Ottawa:MI/IAC. 1996.

Lozoff B, Jimenez E, Smith JB. Double burden of iron deficiency in infancy and low socio-economic status: a longitudinal analysis of cognitive test scores to age 19 years. Arch Pediatr Adolesc Med. 2006;160:1108-13.

Ma Tai, Lu T, Tan U, Chen B, Zhu HI. The present status of endemic goitre and endemic cretinism in China. Food Nutr Bull. 1982;4:13-19.

Maberly GF, Eastman G, Waite KV et al. The role of cassava. In: Ui N, Torizuka K, Nagataki S, Miyai K (eds.). Current problems in thyroid research. Amsterdam: Excerpta Medica. 1983;605:341-4.

Mahalanabis D. Breast feeding and vitamin A deficiency among children attending a diarrhoea treatment centre in Bangladesh: a case-control study. Br Med J. 1991;303:493-6.

Mahboob Ali M, Darnton-Hill I. Manual for the ordering, distribution, monitoring and assessment of each round: vitamin A capsule distribution. Blindness Prevention Programme of Bangladesh. Draft. 1988.

Malinow MR, Duell PB, Hess DL, Anderson PH, Kruger WD, Phillipson BE, Gluckmen RA et al. Reduction of plasma homocysteine levels by breakfast cereal fortified with folic acid in patients with coronary heart disease. New Engl J Med. 1998;338:1009-15.

Mangasaryan N. Global progress towards sustained elimination of iodine deficiency: lessons learnt from salt iodization programs and monitoring. Presented at the Micronutrient Forum. Istanbul, Turkey. April 2007.

Mangasaryan N, de Benoist B, Darnton-Hill I, Bagriansky J. Achieving the goal of sustained elimination of iodine deficiency by the year 2005: successes and challenges. In: Vorster HH, Blaauw R, Dhansay MA, Kuzwayo PMN, Moeng TL, Wentzel-Viljoen E. (eds.). Nutrition Safari for Innovative Solutions. Proc 18th Int Congress Nutr, Durban, South Africa, Ann Nutr Metab. 2005: CDRom available from Karger:Basel. 2005:6pp.

Mannar MGV. Public-private partnerships for improved nutrition: how do we make them work for the public good? Standing Committee on Nutrition of the UN System. Geneva:SCN News. 2003;26:4-7.

Mannar V, Mason JB. Preface: lessons from successful micronutrient programs. Food Nutr Bull. 2004;25:3-4.

Marsh R (with Helen Keller International). Home gardening in Bangladesh: an evaluation report. Dhaka:HKI/AVDRC. Unpublished. 1993.

Marsh R. Household food security through home gardening- evidence from Bangladesh. In Heidhues, Fadani (eds.). Food security and innovations: successes and lessons learned. Frankfurt:Peter Lang Press. 1997.

Marsh R. Building on traditional gardening to improve household food security. Rome: FAO. Food Nutr Agric. 1998;22:4-21.

Martines J, Paul VK, Bhutta ZA, Koblinsky M, Soucat A, Walker N, Bahl R, Fogstad H, Costello A, for the Lancet Neonatal Survival Survival Steering Team. Neonatal survival: a call for action. Lancet. 2005; March 3:43-51 (published online, hard copy version). Available from: http://image.thelancet.com/extras/05art1216web.pdf

Mason E. cited in Peeling R, Heymann D, Mason E. Applying best practices to make programmes work. WHO News. Bull World Health Org. 2006;84:594-6

Mason J, Hunt J, Parker D, Jonsson U. Investing in child nutrition in Asia. Manila:Asian Development Bank. Asian Devel Rev. 1999;17:nos.1&2.

Mason J, Lotfi M, Dalmiya N, Sethuranam K, Deitchler M. The Micronutrient Report: current progress and trends in the control of vitamin A, iodine, and iron deficiencies. University of Tulane School of Public Health & Tropical Medicine/Micronutrient initiative/UNICEF. Ottawa:International Development Research Centre. 2001.

Mason J, Musgrove P, Habicht J-P. At least one-third of poor countries' disease burden is due to malnutrition. Disease Control Priorities Project, Fogarty International Center, Bethesda, Maryland: NIH. 2003;DCPP Working paper no.1:19pp.

Mason J, Deitchler M, Mathys E, Winichagoon P, Tuazon MA. Lessons from successful micronutrient programs. Part III: program impact. Food Nutr Bull. 2004a;25:53-78.

Mason J, Deitchler M, Soekirman, Martorell R (eds.). Successful Micronutrient Programs. Special issue. Food Nutr Bull. 2004b;25:(1):3-88.

Mason J, Bailes A, Beda-Andourou M, Copeland N, Curtis T, Deitchler M, Foster L, Hensley M, Horjus P, Johnson C, Mendez A, Munoz M, Rivers J, Vance G. Recent trends in malnutrition in Developing Regions: vitamin A deficiency, anemia, iodine deficiency, and child underweight. Food Nutr Bull. 2005a;26:59-162.

Mason J, Rivers J, Helwig C (guest eds.). Recent trends in malnutrition in developing regions: vitamin A deficiency, anemia, iodine deficiency and child underweight. Micronutrient Initiative Special Section Reprint. Food Nutr Bull. 2005b;26:5-110.

McGuire J, Galloway R. Enriching Lives. Overcoming vitamin and mineral malnutrition in Developing Countries. Washington, DC: World Bank. 1994.

McLaren DS. The great protein fiasco. Lancet. 1974;ii:93-6.

McLaren DS. Nutrition planning: the poverty of holism. Nature. 1977;267:742.

McLaren DS, Oomen HAPC, Escapini H. Ocular manifestations of vitamin-A deficiency in Man. Bull Wld Health Org. 1966;34:257-361.

McLaren DS, Loveridge N, Duthie G, Bolton-Smith C. Fat-soluble vitamins. In: Garrow JS, James WPT (eds.). Human Nutrition and Dietetics. 9th edition. Singapore: Churchill Livingstone/Longman. 1993:13:208-38.

McLean E, Egli I, Cogswell M, de Benoist B, Wojdyla D. Worldwide prevalence of anemia in pre-school aged children, pregnant women and non-pregnant women of reproductive age. In:Kraemer K, Zimmermann M (eds.). Nutritional anaemia. Basel:Sight & Life Press. 2007;1:1-12.

McMichael AJ. Impact of climatic and other environmental changes on food production and population health in the coming decades. Proc Nutr Soc. 2001;60:195-201.

McMichael P. The impact of globalisation, free trade and technology on food and nutrition in the new millennium. Proc Nutr Soc. 2001;60:215-20.

Mebrahtu T, Stoltzfus RJ, Chwaya HM, Jape JK, Savioli L, Montresor A, Albonico M, Tielsch JM. Low-dose daily iron supplementation for 12 months does not increase the prevalence of malarial infection or density of parasites in young Zanbari children. J Nutr. 2004;134:3037-41.

Mehotra S. Child malnutrition and gender discrimination in South Asia: is the worst malnutrition linked to the worst gender discrimination in the world? In:Thakur R (ed.). South Asia and the UN. Tokyo:UNU Press. 2004;chp20:315-34.

Meinzen-Dick RS. Property rights for empowering low-income women. In: Quisumbing AR, Mienzen-Dick RS (eds.). Empowering women to achieve food security. 2020 Vision for Food, Agriculture, and the Environment. Washington, DC:IFPRI. IFPRI: Focus 6. 2001:20pp.

Mele L, West KP, Jr., Kusdiono, et al. Nutritional and household risk factors for xerophthalmia in Aceh, Indonesia: a case-control study. Am.J.Clin.Nutr. 1991;53:1460-65.

Melse-Boonstra A, de Pee S, Martini E, Sari M, Kosen S, Muhilal, Bloem MW. The potential of various foods to serve as a carrier for micronutrient fortification, data from remote areas in Indonesia. Euro J Clin Nutr. 2000;54:822-7.

Meskel Balcha H. Experience of World Vision Ethiopia Micronutrient program in promoting production of vitamin A-rich foods. In:Abstracts of a Workshop on long-term food-based approach towards eliminating vitamin A deficiency in Africa. MRC (South Africa)/UNU/IUNS. November 2000:25.

MI. Ending Hidden Hunger. 1991. Micronutrient Initiative:Ottawa. www.micronutrient.org (accessed 4 March 2003).

MI. Food fortification to end micronutrient malnutrition: State of the art. Ottawa:MI. 1997.

MI (Ross J, Horton S). Economic consequences of iron deficiency. Ottawa:MI Micronutrient Initiative. 1998.

MI. The Micronutrient Initiative. New solutions for hidden hunger. 2007 http://www.micronutrient.org (accessed 6 March 2007).

MI/UNICEF/ISO/USAID/Swaziland Sugar Assoc. Sugar Fortification to End Vitamin A Deficiency in Southern and Eastern Africa. 1999. http://idrinfo.idrc.ca/archive/corpdocs/117071/117071.txt (accessed 23 June 2006)

MI/UNICEF. Vitamin and Mineral Deficiency. A global report. Ottawa: Micronutrient Initiative. 2003. www.micronutrient.org (accessed 12 January, 2005).

MI/UNICEF. Improving protection for young children against vitamin A deficiency and its impacts on child mortality and morbidity: an analysis of twenty assessments of national vitamin A supplementation programs by UNICEF and the Micronutrient Initiative. Ottawa:MI. Unpublished draft. 2004:26pp.

MI/UNICEF (Aguayo V, Bégin F, Boy E, Codling K, Darnton-Hill, Dalmiya N, Fryars M, Gorstein J, Greig, A, Laviolette L,Marshall C, van Ameringen M). Life beyond NIDs? Harnessing regular health services to protect all children against vitamin A deficiency. A summary draft analysis. UNICEF/MI. Unpublished.

Milio N. Promoting health through structural change: analysis of the origin and implementation of Norway's farm-food-nutrition policy. Soc Sci Med. 1981;15A:721-34.

Miller DS, Holt JFJ. The Ethiopian famine. Proc Nutr Soc. 1975;34:167.

Miller del Rosso J. investing in nutrition with World Bank assistance. Washington,DC:The International Bank for Reconstruction and Development/The World Bank. 1992.

Mitra M, Darnton-Hill I. Nutrition education in the prevention of vitamin A deficiency and nutritional blindness in Bangladesh. In: Moyal MF (ed). Diet and Life Style: New technology. London & Paris:John Libby Eurotext. 1988:413-20.

Molyneux DH, Nantulya VM. Linking disease control programmes in rural Africa: a pro-poor strategy to reach Abuja targets and millennium development goals. Br Med J. 2004;328:1129-32.

Mora JO, Dary O. Strategies for prevention of micronutrient deficiency through food fortification: lessons learned from Latin America. Presented at the 9th World Congress of Food Science and Technology. Budapest. 1995.

Mora JO, Dary O, Chinchilla D, Arroyave G. Vitamin A sugar fortification in Central America: Experiences and lessons learned. Washington, DC:MOST/USAID/INCAP/PAHO. 2000.

Mora JO, Nestel PS. Improving prenatal nutrition in developing countries: strategies, prospects, and challenges. Am J Clin Nutr. 2000;71:1353S-63S.

Moser KA, Leon DA, Gwatkin DR. How does progress towards the child mortality millennium development goal affect inequalities between the poorest and least poor? Analysis of demographic and health survey data. Br Med J. 2005;33:1180-3.

MOST. A strategic approach to anemia control. MOST, USAID Micronutrient Program. Arlington,VA:ISTI. 2004.

Muhilal, Permaesih D, Idjradinata YR, Muherdiyantiningsih, Karyadi D. Vitamin A-fortified monosodium glutamate and health, growth, and survival of children: a controlled field trial. Am J Clin Nutr. 1988;48:1271-6.

Muhilal, Tarwotjo I, Kodyat B, Herman S, Permaesih D, Karyadi D, Wilbur S, Tielsch JM. Changing prevalence of xerophthalmia in Indonesia, 1977-1992. Euro J Clin Nutr. 1994;48:708-14.

Murphy SP, Allen LH. Nutritional importance of animal source foods. J Nutr. 2003;133:S2:3932S-5S.

Murray CJL, Lopez AD (eds.). The Global Burden of Disease. A comprehensive assessment of mortality and disability from disease, injury and risk factors in 1990 and projected to 2020. Geneva:World Health Organization. 1996.

National Research Council. Recommended Dietary Allowances. Washington, DC: National Academy Press. 1989.

Nemer L, Gelband H, Jha P. The evidence base for interventions to reduce malnutrition in children under five and school-age children in low and middle-income countries. CMH Working Paper Series No. WG5:11. Commission on Macroeconomics and Health. Geneva:World Health Organization. 2001.

Nestel P. Food fortification in developing countries. New York:USAID/VITAL. 1993.

Nestel P, Davidsson L. Anemia, iron deficiency, and iron deficiency anemia. INACG publication. Washington, DC:ILSI. 2002.

Nestle M. Genetically engineered ‘golden’ rice unlikely to overcome vitamin A deficiency. J Amer Diet Assoc. 2001;101:289-90.

Network for the Sustainable elimination of IDD. (Mannar MGV, Dunn JT). Iodized salt for the elimination of iodine deficiency disorders. 1995:1-114. Available from: http://206.191.51.240/documents/Iodized%20Salt%20for%20the%20Elimination%20of%20IDD.pdf (accessed Septemeber 14, 2005).

Neumann CG. Background to Symposium on food-based approaches to combating micronutrient deficiencies in children in Developing Countries. J Nutr. 2007;137:1091-2.

Neumann CG, Murphy SP, Gewa C, Grillenberger M, Bwibo NO. Meat supplementation improves growth, cognitive, and behavioral outcomes in Kenyan children. J Nutr. 2007;137:1119-23.

New York Times (Editorial). Cow politics. The New York Times. 2005;Oct27:2pp.

NH&MRC (Australian National Health and Medical Research Council). Report of the 177th Session - Sydney, June 1994. Summary: NHMRC Council session report. 2003. http://www.nhmrc.gov.au/publications/reports/_files/117th.pdf (accessed March 25, 2007).

Nicolas G, Bennoun M, Porteu A**,** Mativet S, Beaumont C, Grandchamp B, Sirito M, Sawadogo M, Kahn A, Vaulont S. Severe iron deficiency anemia in transgenic mice expressing liver hepcidin. Proc Natl Acad Sci USA. 2002;99:4596-601.

Nutriview. Focus on Africa: Investing in nutrition for a continent's future prosperity. Basel: Roche Vitamins. 2001;4:5-7.

Oakley GP, Bell KN, Weber MB. Recommendations for accelerating global action to prevent folic acid-preventable birth defects and other folate-deficiency diseases: meeting of experts on preventing folic acid-preventable neural tube defects. Birth Defects Res. 2004;70:Part A:835-7.

Oakley GP, Mandel JS. Folic acid fortification remains an urgent health priority. Br Med J. 2004;329:1376.

Oliveira MA, Zepeda Bermudez JA, Costa Chavez G, Velásquez G. Has the implementation of the TRIPS Agreement in Latin America and the Caribbean produced intellectual property legislation that favours public health? Bull World Health Org. 2004;82:815-21.

Olsen JA. Vitamin A. In: Zeigler EE, Filer LJ (eds.). Present knowledge in Nutrition. 7th ed. Washington,DC:ILSI Press. 1996.

OMNI (Darnton-Hill I, Canova K, Bolasny D). Final report: 1993-1998. The OMNI Experience: using global lessons to move local programs. Opportunities for Micronutrient Interventions- a fully USAID-funded Project. Arlington VA:John Snow Inc. 1998.

Oniang'o R, Mukudi E. Nutrition and gender. In: Nutrition: A Foundation for Development. Geneva:ACC/SCN. 2002.

Oomen HAPC. Report on survey of Xerophthalmia and Keratomalacia caused by hypovitaminosis A carried out in South and East Asia.Geneva:World Health Organization. MHO/PA. 1963.

Oomen HAPC. Vitamin A deficiency. In: Beaton GH, Bengoa JM (eds.). Nutrition in Preventive Medicine. WHO Monogr Ser No. 62. Geneva: World Health Organization. 1976.

Oomen HAPC, McLaren DS, Ecapini H. Epidemiology and public health aspects of hypovitaminosis A. A global survey of xerophthalmia. Trop Geogr Med. 1964;4:271-315.

Oomen HAPC, ten Doesschate J. The periodicity of xerophthalmia in South and East Asia. Ecol Food Nutr. 1973;2:207-217.

Ooms G. Health development versus medical relief: the illusion versus the irrelevance of sustainability. PloS Med. 2006;3:e345:1202-5.

Ooms G, Derderian K, Melody D. Do we need a World Health Insurance to realize the Right to Health? PLoS Med. 2006;3:e530:2171-6.

Oso OO, Abiodun PO, Omotade OO, Oyewole D. Vitamin A status and nutritional intake of carotenoids of pre-school children in Ijaye Orile commuinity in Nigeria. J Trop Pediatr. 2003;49:42-7.

Packer G. Dreaming of democracy. The New York Times magazine. 2000 March 2:44(9pp).

Pak D, Darnton-Hill I. Achieving sustainable vitamin A elimination. New York:UNICEF. Internal intern paper. Unpublished 2006.

Pandav CS. Sustaining elimination of iodine deficiency disorders in South Asian countries. International Health Oration, 28th Annual PHAA Conference, Western Australia. Public Health Association of Australia. Monograph. 1996:1-25.

Peeling R, Heymann D, Mason E. Applying best practices to make programmes work. WHO News. Bull Wld Hlth Org. 2006;84:594-6

Pelletier DL, Frongillo EA. Changes in child survival are strongly associated with changes in malnutrition in developing countries. J Nutr. 2003;133:107–19.

Pepping F, van Der Giezen AM, de Jonge KI, West CE. Food consumption of children with and without xeropththalmia in rural Tanzania. Trop Geogr Med.1989;41:14-21.

Persson LA, Eneroth H, Ekström E-C. Multiple micronutrient supplementation during pregnancy. A review of effects on birth size, maternal haemoglobin, and perinatal mortality demonstrated in trials in Bangladesh, Guinea-Bissau and Pakistan. Draft report to UNICEF. 2004.

Pharaoh POD, Connolly DC. A controlled trial of iodinated oil for the prevention of endemic cretinism: a long term follow-up. Int J Epidemiol. 1987;16:68-73.

Phillips M, de Mattos A. What is the role of international agencies in the micronutrient sector? Food Nutr Bull. 2007;28:S204-S12.

PMNCH (Partnership for Maternal, Neonatal and Child Survival). Tracking progress in child survival. Countdown to 2015 Conference. Child Survival. London School of Hygiene and Tropical Medicine. London, UK. December, 2005. Available from: http://www.pmnch.org/ (accessed July 4, 2006).

Pollitt E. The developmental and probabilistic nature of the functional consequences of iron-deficiency anemia in children. J Nutr. 2001;131:669S-75S.

Pollitt E, Gorman KS, Engle PL, Rivera JA, Martorell R. Nutrition in early life and the fulfillment of intellectual potential. J. Nutr. 1995;125(4 Suppl):1111S-8S.

Prah Ruger J. The changing role of the World Bank in global health. Am J Publ Hlth. 2005;95:60-70.

Prentice AM, Ghattas H, Doherty C, Cox S. Iron metabolism and malaria. Background paper for the WHO Expert Consultation on iron supplementation in high malaria areas. Lyon:UNESCO.

Unpublished. 2006 (but available from the MRC International Nutrition Group, London School of Hygiene & Tropical Medicine, London, UK).

Puska P, Tuomilehto J, Nissinen A, Vartiainen E. The North Karelia Project. 20 year results and experiences. Helsinki:National Public Health Institute (KTI). 1995.

Quinn VJ, Guyon AB, Schubert JW, Stone-Jiminez M, Hainsworth MD, Martin LH. Improving breastfeeding practices on a broad scale at the community level: Success stories from Africa and Latin America. J Hum Lact. 2005;21:345-54.

Quisumbing AR, Maluccio JA. Intrahousehold allocation and gender relations: New empirical evidence from four developing countries. Washington, DC:International Food Policy Research Institute. FCND Discussion Paper No. 84. 2000:80pp.

Quisumbing AR, Haddad L, Peña C. Are women overrepresented among the poor? An analysis of poverty in ten developing countries. Washington, DC:International Food Policy Research Institute. FCND Discussion Paper No. 115. 2001:66pp.

Rahmathullah L, Tielsch JM, Thulasiraj RD, Katz J, Coles C, Devi S, John R, Prakash K, Sadanand AV, Edwin N, Kamaraj C. Impact of supplementing newborn infants with vitamin A on early infant mortality: community-based randomised trial in southern India. Br Med J. 2003;327:254-9.

Rahmathullah L, Underwood BA, Thulasiraj RD, Milton RC, Ramaswamy K, Rahmathullah R, Babu G. Reduced mortality among children in Southern India receiving a small weekly dose of vitamin A. N.Eng.J.Med. 1990;323:929-35.

Ramakrishnan U, Darnton-Hill I. Vitamin A deficiency disorders: assessment and control of VADD. J Nutr. 2002;132(9S):2947S-53S.

Rao S, Yajnik CS, Kanade A, Fall CHD, Margetts BM, Jackson AA, Shier R, Joshi S, Rege S, Lubree H, Desai B. Intake of micronutrient-rich foods in rural Indian mothers is associated with the size of their babies at birth: Pune Maternal Nutrition Study. J Nutr. 2001:131:1217-24.

Rassas B, Nakamba PM, Mwela CM, Mutwmwa RI, Mutemwa BM, Siamusantu W. Cost analysis of the national vitamin A supplementation program in Zambia. MOST Project. Arlington VA:ISTI Inc./USAID. August 2003.

Rassas B, Hottor JK, Anerkai OA, Kwame MM, Agble R, Nyaku A. Cost analysis of the national vitamin A supplementation program in Ghana. MOST Project. Arlington VA:ISTI Inc./USAID. March 2004.

Ray JG, Wyatt PR, Thompson MD, Vermeulen MJ, Meier C, Wong P-Y, Farrell SA, Cole DEC. Vitamin B_{12} and the risk of neural tube defects in a folic-acid-fortified population. Epidemiol. 2007;18:362-6.

Rayman MP. The argument for increasing selenium intake. Proc Nutr Soc. 2002;61:203-15.

Reddy V. Control of vitamin A deficiency and blindness: the Indian experience. In: Darnton-Hill I (ed.). Vitamin A Deficiency in Bangladesh: Prevention and control. Dhaka:HKI. 1989;chp2.6:124-9.

Rice AL. Postpartum vitamin A supplementation: evaluating the evidence for action. A2Z Technical Brief. A2Z Micronutrient Project of USAID. Washington,DC:AED. 2007.

Rice AL, Stoltzfus RJ, de Francisco A, Chakraborty J, Kjolhede CL, Wahed MR. Maternal vitamin A or β-carotene supplementation in lactating Bangladeshi women benefits mothers and infants but does not prevent subclinical deficiency. J Nutr. 1999;129:356-65.

Rice AL, Sacco L, Hyder A, Black RE. Malnutrition as an underlying cause of childhood deaths associated with infectious diseases in developing countries. Bull Wld Hlth Org. 2000; 78(10):1207-21.

Rice AL, West KP, Black RE. Vitamin A deficiency. In: Ezzati M, Lopez AD, Rodgers A, Murray CJL. (eds.). Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Vol 1. Geneva:World Health Organization. 2004;chp4:211-56.

Richter J. Global public-private 'partnerships': how do we ensure that they are in the public interest? Geneva:Standing Committee on Nutrition of the UN System. SCN News 2003a;26:8-11.

Richter J. 'We the peoples' or 'we the corporations'? Critical reflections on UN-business 'partnerships'. Geneva:Geneva Infant Feeding Association/International baby Food Action Network (GIFA-IBFAN). 2003b. Available from: www.ibfan.org.

Rivera JA, Hotz C, González-Cossío T, Neufeld L, García Guerra FA. The effect of micronutrient deficiencies on child growth: a review of results from community-based supplementation trials. J Nutr. 2003;133:4010S-20S.

Rogers LM, Boy E, Miller JW, Green R, Allen LH. High prevalence of cobalamin deficiency in Guatemalan school children: association with elevated serum methylmalonic acid and plasma homocysteine, and low plasma holotranscobalamin II concentrations. Am J Clin Nutr. 2003;77:433-40.

Roos N, Wahab MA, Chamman C, Thilsted SH. The role of fish in food-based strategies to combat vitamin A and mineral deficiencies in Developing Countries. J Nutr. 2007;137:1106-9.

Rosa FW, Wilk AL, Kelsey FO. Teratogen update: vitamin A congeners. Teratology. 1986;33:355-64.

Rosegrant MW, Paisner MS, Meijer S, Witcover J. 2020 Global Food Outlook. Trends, alternatives, and choices. IFPRI Food policy report. Washington,DC:International Food Policy Research Institute. 2001.

Rosen DS, Sloan NL, Delrosar A, Delapza TC. Risk factors for vitamin A deficiency in rural areas of the Philippines. J Trop Pediatr. 1994;40:82-87.

Ross J, Horton S. Economic consequences of iron deficiency. Ottawa:The Micronutrient Initiative 1998.

Roy CN, Mak HH, Akpan I, Losyev G, Zurakowski D, Andrews NC. Hepcidin antimicrobial peptide transgenic mice exhibit features of the anemia of inflammation. Blood. 2007;109:4038-44.

Ruel MT. Can Food-Based Strategies Help Reduce Vitamin A and Iron Deficiencies?: A review of recent evidence. Washington,DC:International Food Policy Research Institute. 2001.

Ruel MT, Levin CE. Assessing the potential for food-based strategies to reduce vitamin A and iron deficiencies: a review of recent evidence. International Food Policy Research Institute. IFPRI Discussion Paper 92. 2000.

Sachs J (ed.). WHO Report on Macroeconomics and Health. Macroeconomics and health: investing in health for economic development. Geneva:WHO. 2001.

Sachs JD, McArthur JW. The Millennium Project: a plan for meeting the Millennium Development Goals. Lancet 2005;365(9456):347-53.

Sanghvi TG. Economic rationale for investing in micronutrient programs. OMNI Project 1993. Reprinted as MOST (the USAID Program on Micronutrients) Policy brief No.89.1995. http://www.mostproject.org/pubs2.htm (accessed 15 April 2007)

Sari M, Bloem MW, de Pee S, Schultink WJ, Sastroamidjojo S. Effect of iron-fortified candies on the iron status of children aged 1-4y in East Jakarta, Indonesia. Am J Clin Nutr. 2001;73(6):1034-9.

Sazawal S, Black RE, Bhan MK, Bhandari N, Sinha A, Jalla S. Zinc supplementation in young children with acute diarrhoea in India. N Engl J Med. 1995;338:839-44.

Sazawal S, Black RE, Ramsan M, Chwaya HM, Stoltzfus RJ, Dutta A, Dhungra U, Kabole I, Deb S, Othman MK, Kabole F. Effects of routine prophylactic supplementation with iron and folic acid on admission to hospital and mortality in preschool children in a high malaria transmission setting: community-based, randomized, placebo-controlled trial. Lancet. 2006;367:133-43.

Schellenberg J, Adam T, Mshinda H, Masanja H, Kabadi G, Mukasa O, John T, Charles S, Nathan R, Wilczynska K. Effectiveness and cost of facility-based Integrated Management of Childhood Illness (IMCI) in Tanzania. Lancet. 2004;364:1583-94.

Schémann JF, Banou A, Malvy D, Guindo A, Traore L, Momo G. National immunization days and vitamin A distribution in Mali: has the vitamin A status of pre-school children improved? Publ Health Nutr. 2002;6:233-40.

Schmidt MK, Muslimatun S, West CE, Schultink W, Hautvast JGAJ. Vitamin A and iron supplementation of pregnant Indonesian women benefits the vitamin A status of their infants, but still may need vitamin A supplementation or increased dietary intake. Br J Nutr. 2001;86:607-15.

Scholz BD, Gross R, Schultink W, Sastroamidjojo S. Anaemia is associated with reduced productivity of women workers even in less-physically-strenuous tasks. Br J Nutr. 1997;77:47-57.

Schuftan C, Ramalingaswami V, Levinson FJ. Micronutrient deficiencies and protein-energy malnutrition. Letter. Lancet. 1998;351:1812.

Schultink W. Iron supplementation: compliance of target groups and frequency of tablet intake. Food Nutr Bull. 1996;17:22-6.

Schultink W, Gross R, Gliwitzki M, Karyadi, Matulessi P. Effect of daily vs twice weekly iron supplementation in Indonesian preschool children with low iron status. Am J Clin Nutr. 1995;61:111-5.

Schultink W, Merzenich M, Gross R, Shrimpton R, Dillon D. Effects of iron-zinc supplementation on the iron, zinc and vitamin A status of anaemic pre-school children in Indonesia. Food Nutr Bull. 1997;18:311-7.

SCN. Nutrition goals and targets. Geneva:SCN News. 2001;22:(July):5-31.

SCN. 5th Report on the World Nutrition Situation. Nutrition for improved development outcomes. UN System Standing Committee on Nutrition of the UN System. Geneva:World Health Organization. 2004.

SCN/WHO/UNICEF. Multiple micronutrient compared to iron/folic acid supplementation among presumably HIV negative women during pregnancy: an SCN/WHO/UNICEF meeting to review results of randomized controlled trials. Geneva:World Health Organization. June 2006.

Scrimshaw NS. Synergistic and antagonistic interactions of nutrition and infection. FASEB J. 1966;25:1679-81.

Scrimshaw NS, San Giovanni JP. Synergism of nutrition, infection, and immunity: an overview. Am J Clin Nutr. 1997; 66 (suppl): 464-77.

Semba RD. Vitamin A, immunity, and infection. Clin Infect Dis. 1994;19:489-99.

Semba RD. Vitamin A as "anti-infective" therapy, 1920-1940. J Nutr. 1999;129:783-91.

Semba RD. Iodine deficiency disorders. In: Semba RD, Bloem MW (eds.). Nutrition and Health in Developing Countries. Preventive Nutrition Series. Totowa, NJ:Humana Press. 2001a;chp14:343-63.

Semba RD. Nutrition and development: a historical perspective. In: Semba RD, Bloem MW (eds.). Nutrition and health in Developing Countries. Totowa, NJ:Humana Press. 2001b;1-30.

Semba RD, Miotti PG, Chipangwi JD, Saah AJ, Canner JK, Dallabetta GA, Hoover DR. Maternal vitamin A deficiency and mother to child transmission of HIV-1. Lancet. 1994;343:1593-7.

Semba RD, Susatio B, Muhilal, Natadisastra G. The decline of admissions for xeropthalmia at Cicendo Eye Hospital, Indonesia, 1981-1992. Int Ophthalmol. 1995;19:39-42.

Semba RD, Gray GE. Human immunodeficiency virus infection. In: Semba RD, Bloem MW (eds.). Nutrition and Health in Developing Countries, Preventive Nutrition Series. Totowa, NJ: Humana Press. 2001;chp10:237-66.

Semba R, Bloem MW (eds.). Nutrition and Health in Developing Countries. 2nd ed. Totowa, NJ:Humana Press. 2007. In press.

Sethuraman K, Dalmiya N, Mason J, Lotfi M, Alnwick D. Progress in controlling vitamin A deficiency. UNICEF/Tulane University/Micronutrient Initiative. Draft. 1997.

Shankar A. Malaria. In: Semba RD, Bloem MW (eds.). Nutrition in Developing Countries. Totowa, NJ:Humana Press. 2001;chp8:177-207.

Shankar A, Gittelsohn J, West KP, Jr., Stallings R, Gnywali T, Faruque F. Eating from a shared plate affects food consumption in vitamin A-deficient Nepali children. J Nutr. 1998;128:1127-33.

Shankar A, Prasad AS. Zinc and immune function: the biological basis of altered resistance to infection. Am J Clin Nutr. 1998; 66 (suppl): S447-S63.

Sharman A. Anaemia in Central Asia: demographic and health survey experience. Food Nutr Bull. 1998;19:307-17.

Shetty S. The Millennium Campaign: getting governments to keep their promises. Development. 2005;48:25-9.

Shrimpton R. Food consumption and dietary adequacy according to income in 1200 families, Manaus, Amazonas, Brazil. Archivos Latinoamericanos de Nutricion 1984;34:615-29.

Shrimpton R. Evidence vs. rights-based decision making for nutrition. Proc Nutr Soc. 2003;62:553-62.

Shrimpton R, Macleod-Omawale J, Metz P, Belbase K. UNICEF nutrition Portfolio Review (1980-1999). A contribution to the World Bank/UNICEF Nutrition Assessment. UNICEF:New York. Unpublished. September 2002.

Shrimpton R, Allen L (eds.). International Research on Infants Supplementation (IRIS): randomized controlled trials of micronutrient supplementation during infancy. J Nutr. 2005;135(3S):628S-630S.

Shrimpton R, Dalmiya N, Darnton-Hill I, Gross R. Micronutrient supplementation in pregnancy. Letter. Lancet. 2005; 366:2001-2.

Shrimpton R, Gross R, Darnton-Hill I, Young M. Zinc deficiency: what are the most appropriate interventions? Br Med J. 2005;330:347-9.

Sifri Z, Darnton-Hill I, Baker SK, Ag Bendech Md, Aguayo VM. A concise overview of micronutrient deficiencies in Africa and future directions. Africa J Food Nutr Sci. 2002;2:78-85.

Singhal N, Austin J. A clinical review of micronutrients in HIV infection. J Int Assoc Physicians AIDS Care (Chic Ill). 2002;1(2):63-75.

Sinha DP, Bang FB. Seasonal variation in signs of vitamin-A deficiency in rural West Bengal children. Lancet. 1973;2:228-31.

Sinha DP, Bang FB. The effect of massive doses of vitamin A on the signs of vitamin A deficiency in preschool children. Am J Clin Nutr. 1976;29:110-15.

Smitasiri S, Cavalli-Sforza LT, Berger J, Viteri F. Summary: weekly iron-folic acid supplementation of women of reproductive age: impact overview, lessons learned, expansion plans and considerations towards achievement of the Millennium Development Goals. Nutr Rev. 2005;63(II):S152-8.

Smith L. Can FAO's measures of chronic undernourishment be strengthened? IFPRI Discussion Paper briefs- Discussion paper 44. Food Consumption and Nutrition Division of the International Food Policy Research Institute. Washington, DC: IFPRI. 1998.

Smith L, Haddad L. Overcoming child malnutrition in developing countries: past achievements and future choices. Washington, DC:International Food Policy Research Institute. IFPRI 2020 Brief No.64. 2000.4pp. http://www.ifpri.org/2020/briefs/number64.htm (accessed February 7, 2006)

Smith L, Ramakrishnan U, Ndiaye A, Haddad L, Martorell R. The importance of women's status for child nutrition in Developing Countries. Washington, DC: International Food Policy Research Institute/Department of International Health, Emory University. IFPRI Research Report 131. 2003.

Solomons NW. There needs to be more than one way to skin the iodine deficiency disorders cat: novel insights from the field in Zimbabwe. Am J Clin Nutr. 1998;67:1104-5.

Solomons NW. Vitamin A. In: Bowman BA, Russell RM (eds.). Present knowledge in Nutrition. 9th ed. Washington,DC:ILSI Press. 2006;chp12:157-83.

Solon FS, Popkin BM, Fernandez TL, Latham MC. Vitamin A deficiency in the Phillipines: a study of xerophthalmia in Cebu. Am J Clin Nutr. 1978;31:360-8.

Solon FS, Solon MS, Mehansho H, West KP jnr, Sarol J, Perfecto C, Nano T, Sanchez L, Isleta M, Wasantwisut E, Sommer A. Evaluation of the effect of vitamin A-fortified margarine on the vitamin A status of pre-school Filipino children. Euro J Clin Nutr. 1996;56:720-3.

Solon FS, Klemm RDW, Sanchez L, Darnton-Hill I, Craft NE, Christian P, West KP Jr. Evaluation of the efficacy of a vitamin A-fortified wheat-flour bun on the vitamin A status of Filipino schoolchildren. Am J Clin Nutr. 2000;72:738-44.

Solon FS, Fermin LS, Wambangco LS, Solon MA. Vitamin A and iron compound stability in flour and products. In: XXth IVACG Report 25 Years of progress in controlling vitamin A deficiency: looking to the future'. Washington, DC:IVACG/USAID/ILSI Research Foundation. J Nutr. 2002; Abstracts:20:2964S.

Sommer A. Nutritional Blindness, Xerophthalmia and Keratomalacia. New York: Oxford University Press, 1982.

Sommer A. Vitamin A Deficiency and its Consequences: A Field Guide to Their Detection and Control. 3rd ed. Geneva: World Health Organization. 1995.

Sommer A, Tarwotjo I, Hussaini G, Susanto D, Soegiharto T. Incidence, prevalence and scale of blinding malnutrition. Lancet. 1981;1:1407-08.

Sommer A, Hussaini G, Tarwotjo I, Susanto D. Increased mortality in children with mild vitamin A deficiency. Lancet. 1983;2:585-8.

Sommer A, Katz J, Tarwotjo I. Increased risk of respiratory disease and diarrhea in children with preexisting mild vitamin A deficiency. Am J Clin Nutr. 1984;40:1090-5.

Sommer A, West KP Jnr. Vitamin A deficiency, health, survival and vision. New York: Oxford University Press. 1996.

Sommer A, Davidson FR, Ramakrishnan U, Darnton-Hill I. 25 years of progress in controlling vitamin A deficiency: looking to the future. Proc XX IVACG Meeting. (Guest editors). J Nutr. 2002:132(9S):2845S-990S.

Sommer A, Davidson FR. Assessment and control of vitamin A deficiency: The Annecy Accords. In: 25 years of progress in controlling vitamin A deficiency: looking to the future. Proc XX IVACG Meeting. J Nutr. 2002;132:2845S-50S.

Stanbury J (ed.). The damaged brain of iodine deficiency. New York: Cognizant Communication Corporation. 1994:v-vii.

Stanton BF, Clemens JD, Wojtyniak B, Khair T. Risk factors for developing mild nutritional blindness in urban Bangladesh. Am J Dis Child. 1986;140:584-8.

Staubli Asobayire F, Adou P, Davidsson L et al. Prevalence of iron deficiency, with and without concurrent anaemia, in population groups with high prevalence of malaria and other infections: a study in Cote d'Ivoire. Am J Clin Nutr. 2001;74:776-82.

Stein AJ, Qaim M. The human and economic costs of hidden hunger. Food Nutr Bull. 2007;28:125-34.

Stevens C, Kennan J. Food aid and trade. In: Devereux S, Maxwell S (eds.). Food security in sub-Saharan Africa. Pietermaritzburg:University of Natal Press. 2001.

Stoltzfus RJ. Summary: implications for research and programs. J Nutr. 2001a;131:697-701S.

Stoltzfus RJ. Defining iron-deficiency anemia in public health terms: a time for reflection. J Nutr. 2001b;131:565S-7S.

Stoltzfus RJ. Iron deficiency: global prevention and consequences. Food Nutr Bull. 2003;24:S97-S101.

Stoltzfus RJ, Hakimi M, Miller KW, Rasmussen KM, Dawiesah S, Habicht J, Dibley MJ. High dose vitamin A supplementation of breast feeding Indonesian mothers: effects on the vitamin A status of mother and infant. J Nutr. 1993;123:666-675.

Stoltzfus RJ, Chwaya HM, Tielsch JM, Schulze KJ, Albonico M, Savioli L. Epidemiology of iron deficiency anemia among Zanzibari schoolchildren: the importance of hookworms. Am J Clin Nutr. 1997;65:153-9.

Stoltzfus RJ, Dreyfus, ML. Guidelines for the use of iron supplements to prevent and treat iron deficiency anemia. INACG/WHO/UNICEF. Washington,DC:ILSI Press. 1998.

Stoltzfus RJ, Chway HM, Montresor A, Tielsch JM, Jape JK, Albonico M, Savioli L. Low dose daily iron supplementation improves iron status and appetite but not anemia, whereas quarterly anthelminthic treatment improves growth, appetite and anemia in Zanzibari preschool children. J Nutr. 2004a;134:348-56.

Stoltzfus RJ, Mullany L, Black RE. Iron deficiency anaemia. In: Ezzati M, Lopez AD, Rodgers A, Murray CJL. (eds.). Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Vol 1. Geneva:World Health Organization. 2004b;chp3:163-210.

Stover PJ, Garza C. Molecular and genetic considerations for long-term nutrition interventions. Asia Pac J Clin Nutr. 2002;11:Suppl6:S129-S36.

Suharno D, West CE, Muhilal, Karyardi D, Hautvast JGAJ. Supplementation with vitamin A and iron for nutritional anaemia in pregnant women in West java, Indonesia. Lancet. 1993;342:1325-8.

Supplefer. Sprinkles for humanitarian aid interventions. Available from: www.MicronutrientSprinkles.org and www.supplefer.org (accessed 14 January 2005).

Tagwireyi J. Time for a change? A field's eye view of donor agency support for nutrition. The Annual Martin J Forman Memorial Lecture. Presented at the NCIH Conference, Arlington, VA, USA. New York:Helen Keller International. 1994.

Talukder A, Bloem MW. Homegardening activities in Bangladesh. Dhaka:Helen Keller International. 1993:1-43.

Talukder A, Kiess L, Huq N, de Pee S, Darnton-Hill I, Bloem MW. Increasing the production and consumption of vitamin A-rich fruits and vegetables: lessons learned in taking the Bangladesh homestead gardening programme to a national scale. Food Nutr Bull. 2000;21:165-72.

Tang AM, Graham NMH, Chandra RK, Saah AJ. Low serum vitamin B-12 concentrations are associated with faster Human Immunodeficiency Virus Type 1 (HIV-1) disease progression. J. Nutr. 1997;127: 345-51.

Tang G, Gu X, Hu S, Xu G, Qin J, Dolnikowski GG, Fjeld CR, Gao X, Russell RM, Yin S. Green and yellow vegetables can maintain body stores of vitamin A in Chinese children. Am J Clin nutr. 1999;70:1069-76.

Tan-Torres Edejer T, Aikins M, Black RE, Wolfson L, Hutubessy R, Evans DB. Achieving the millennium development goals for health: Cost effectiveness analysis of strategies for child health

in developing countries. Br Med J. doi:101136/bmj.38652.550278.7C (published 10 November 2005).

Taylor MJ, Carney S, Goodwin GM, Geddes JR. Folate for depressive disorders: systematic review and meta-analysis of randomized controlled trials. J Psychopharmacol. 2004;18:251-6.

Tee ES, Cavalli-Sforza LT, Kandiah M, Narimah A, Chong SM, Satgunasingan N, Kamarudin L. A study of the effectiveness of iron supplementation in adolescent secondary school girls in Malaysia: preliminary findings. In: Towards achieving nutritional goals of the Asian region. Abstracts of the 7th Asian Congress of Nutrition. Beijing: Chinese Nutrition Society. 1995:127.

Thapa M, Choe R, Retherford R. Evaluation of vitamin A supplementation program showing reduced child mortality of 50%,Trop Med Internat Health 2005;10:782-5.

Thuy PV, Berger J, Davidsson L, Khan NC, Nga TT, Lam NT, Mai TT, Flowers C, Nakanish Y, Cook JD, Hurrell RF & Khoi HH. In: XXth IVACG Report '25 Years of progress in controlling vitamin A deficiency: looking to the future'. Washington, DC:IVACG/USAID/ILSI Research Foundation. Abstracts. F47:30. 2001.

Tielsch JM, Khatry SK, Stoltzfus RJ, Katz J, LeClerq SC, Adhikari R, Mullany LC, Shrestra S, Black RE. Effect of routine prophylactic supplementation with iron and folic acid on preschool child mortality in southern Nepal: community-based, randomized, placebo-controlled trial. Lancet. 2006;367:144-52.

Tielsch JM, West KP, Jr., Katz J, Chirambo MC, Schwab L, Johnson GJ, Tizazu T, Swartwood J, Sommer A. Prevalence and severity of xerophthalmia in southern Malawi. Am J Epidemiol. 1986;124:561-86.

Timmer A. Eliminating iodine deficiency in central Eastern Europe, Commonwealth independent Sates and the Baltics. International Council for Control of Iodine Deficiency Disorders. IDD Newsletter. 2004;20:53-9.

Tjiong R. The Indonesian-MSG-vitamin A fortification project 1977-1995. Jakarta, Indonesia:Hellen Keller International. 1996. Unpublished.

Todd CH, Dunn JT. Intermittent oral administration of potassium iodate solution for the correction of iodine deficiency. Am J Clin Nutr. 1998;67:1279-83.

Toenniessen GH. Crop genetic improvement for enhanced human nutrition. J Nutr. 2002;132:2493S-46S.

Tomkins A. Improving maternal nutrition and pregnancy outcome- The role of micronutrient supplements with special reference to populations that are endemic for HIV. Presented at the UNICEF Regional Nutrition Network Meeting (Eastern & Southern Africa Region). Entebbe, Uganda. 2004:1-12.

Tonascia JA. Meta-analysis of published community trials: impact of vitamin A on mortality. Bellagio Meeting on Vitamin A Deficiency & Childhood Mortality. Proceedings of "Public Health Significance of Vitamin A Deficiency and Its Control." New York: Helen Keller International. 1993:49-51.

Torlesse H, Kiess L, Bloem MW. Association of household rice expenditure with child nutritional status indicates a role for macroeconomic food policy in combating malnutrition. J Nutr. 2003;133(5):1320-5.

Toteja GS, Singh P, Dhillon BS, Saxena BN, Ahmed FU, Singh RP, Prakash B, Vijayaraghavan K, Singh Y, Rauf A, Sarma UC, Gandhi S, Behl L, Mukherjee K, Swami SS, Meru V, Chandra P, Chandrawati , Mohan U. Prevalence of anemia among pregnant women and adolescent girls in 16 districts of India. Food Nutr Bull. 2006;27:311-5.

UN Millennium Project. Investing in Development: A practical plan to achieve the Millennium Development Goals. Overview. Report to the Secretary-General. 2005a.

UN Millennium Project. Who's got the power? Transforming health systems for women and Children. In: Freedman LP, Waldman RJ, de Pinho H, Wirth ME, Chowdhury AM, Rosenfield A. Task Force on Child Health and Maternal Health. New York:UN. 2005b; 1-24.

UN. UN Commmission on sustainable development. www.un.org/esa/sustdev/ (accessed February 2005).

UN. Universal Declaration of Human Rights. Adopted and proclaimed by General Assembly, United Nations. Preamble: Resolution 217 A (III) of 10 December 1948. www.un.org (accessed 29th June 2002).

UN. Convention on the elimination of all forms of discrimination against women. United Nations. 1979. Available from: http://www.un.org/womenwatch/daw/cedaw.

UN. Convention on the Rights of the Child. United Nations. 1989. Available from: http://www.unicef.org/crc/crc.htm

UN. We the peoples: The role of the United Nations in the 21st century. Report by the Secretary-General of the UN, Kofi Annan. 2000a. http://ww.un.org/millennium/sg/report/ch0.pdf (accessed 21 April 2006).

UN. UN Millennium Development Goals. 2000b. http://www.un.org/millenniumgoals/ (accessed 3 February, 2005).

UN. United Nations Millennium Declaration (United Nations General Assembly Resolution 55/2). New York:United Nations. 2000c. www.org/millennium/declaration/ares552pdf (accessed 15 April 2006)

UN. Road map towards the implementation of the United Nations Millennium Declaration: report of the Secretary-General. 56th Session of the General Assembly. (UN document no. A/56/326). New York: UN. 2001.

UN. A world fit for children. 27th Special Session of the General Assembly of the United Nations. New York:UN. A/RES/S-27/2. 2002a.

UN. Implementation of the United Nations Millennium Declaration. Report of the Secretary-General. 57th Session of the General Assembly. (UN document no. A/57/270). New York:UN. 2002b:1-35.

UN. Report of the International Conference on financing for development, Monterrey, Mexico, 18-22 March A/CONF.198/11. 2002c. http://www.un.org/esa/ffd/aconf198-11.pdf (accessed 2 January 2006).

UN. The Millennium Development Goals Report 2006. New York:United Nations. 2006.

UNDP. Human Development Report. 2002. www.undp.org/hdr (accessed 16 January 2003).

UNDP. Global Development report 2003. United Nations Development Programme. New York:UNDP. 2003a.

UNDP. Human Development Report 2003. Millennium Development Goals: a status report. Summary. New York:Oxford University Press for the United Nations Development Programme. 2003b:85-111.

UNDP. Sub-Saharan Africa- The human costs of the 2015 'business-as-usual' scenario. Human Development Report Office. New York:UNDP. 2005. Available from: http://www.undp.org (accessed July 13, 2005)

UNDP. Annual Report 2006: Global partnership for development. New York:UNDP. 2006. http://www.undp.org/publications/annualreport2006/empowering_women.shtml (accessed July 2, 2006).

UNDP. Global Development Report 2006. United Nations Development Programme. New York:UNDP. 2006.

UNICEF. Progress since the World Summit for Children: a statistical review. 2001. http://www.unicef.org/publications/index_6440.html (accessed 29 June 2002).

UNICEF. World declaration on the survival, protection and development of children. The World Summit for Children. New York:UNICEF. 1990a.

UNICEF. Strategy for improved nutrition of Children and Women in Developing Countries. A UNICEF Policy Review. New York: UNICEF. 1990b.

UNICEF/WHO. World Summit for Children- Mid-decade goal: vitamin A deficiency (VAD). UNICEF-WHO Joint Committee on Health Policy. Special Session. Geneva:World Health Organization. JCHPSS/94/2.8 1994a.

UNICEF/WHO. World Summit for Children- Mid-decade goal: iodine deficiency disorders (IDD). UNICEF-WHO Joint Committee on Health Policy. Special Session. Geneva:World Health Organization. JCHPSS/94/2.8 1994b.

UNICEF/WHO. World Summit for Children- Strategic approach to operationalizing selected end-decade goals: reduction of iron deficiency anaemia. UNICEF-WHO Joint Committee on Health Policy. Special Session. Geneva:World Health Organization. JCHP30/95/4.5 1995.

UNICEF. The State of the World's Children: 1998. Focus on Nutrition. New York:Oxford University Press for UNICEF. 1998a.

UNICEF. Progress in controlling vitamin A deficiency. UNICEF/Tulane University/MI. UNICEF:New York. 1998b.

UNICEF. Progress since the the World Summit for Children: A statistical review. New York: UNICEF. 2001a. http://www.unicef.org/publications/index_6440.html (29 June 2002).

UNICEF. A World Fit for Children. II. Review of progress and lessons learned. A/S-27/19/Rev1. 2001b. Available from: www.unicef.org (accessed 12 January 2003).

UNICEF. UN Special Session of the General Assembly on the Child. A World Fit For Children. New York:UNICEF. 2002a.

UNICEF. The State of the World's Children: 2002: leadership: the rate of progress. 2002b. http://www.unicef.org/sowc02summary/table8.html (accessed December 29, 2003).

UNICEF. A World Fit for Children. New York:UNICEF. 2002c.

UNICEF. The State of the World's Children 2003. New York: Oxford University Press for UNICEF. 2003a.

UNICEF. Getting to the roots- mobilizing community volunteers to combat vitamin A deficiency disorders in Nepal. Kathmandu:UNICEF Regional Office for South Asia (ROSA). 2003b.

UNICEF. Progress for Children. A child survival report card. New York:UNICEF. 2004;1:1-22.

UNICEF. The Medium Term Strategic Plan (2006-2009). UNICEF Executive Board document. New York: UNICEF. 2005a.

UNICEF. Progress for Children. A report card on gender parity and primary education. New York:UNICEF. 2005b;2:1-30.

UNICEF. Progress for Children. A report card on nutrition. New York:UNICEF. 2006a;4:1-22.

UNICEF. A world fit for children. New York:UNICEF. 2006b:108pp

UNICEF. (Dalmiya N, Palmer A, Greig A, Darnton-Hill I eds.). Vitamin A supplementation: a decade of progress. Working paper. New York: UNICEF. 2006c.

UNICEF. UNICEF Joint Health and Nutrition Strategy for 2006-2015. Executive Board, First Regular Session, 16-23 January 2006. Item 8 of the provisional agenda. 2006d. Available from: http://www.unicef.org/about/execboard/files/2006-5-part1-bdrept.pdf (accessed 15 July 2006).

UNICEF. The State of the World's Children: 2006. Excluded and invisible. New York: Oxford University Press for UNICEF. 2006e.

UNICEF. Vitamin A Supplementation: Progress for child survival. UNICEF Working Paper. New York: UNICEF. 2006f.

UNICEF. The State of the World's Children: 2007. New York:Oxford University Press for UNICEF. 2007a.

UNICEF. (Dalmiya N, Palmer A). Vitamin A supplementation. A decade of progress. New York:UNICEF. 2007b.

UNICEF. CIDA-UNICEF meeting on Vitamin A supplementation. June 14, 2007. UNICEF Nutrition Section (coordinated by Dalmiya N). Unpublished. 2007c.

UNICEF/MI. Improving protection for young children against vitamin A deficiency and its impacts on child mortality and morbidity. The Micronutrient Initiative:Ottawa. Unpublished. 2004.

UNICEF/MI. Vitamin & Mineral Deficiency. A global progress report. Ottawa:Micronutrient Initiative. 2004.

UNICEF/MI/WHO/CIDA/USAID. A strategy for acceleration of progress in combating vitamin A deficiency: Consensus of an informal technical consultation. New York: UNICEF. 1997.

UNICEF/UNU/WHO Study team. Multiple micronutrient supplementation during pregnancy (MMSDP): efficacy trials. Report of a Meeting. London, organized by the Centre for International Child Health, Institute of Child Health, University College, London and The Micronutrient Initiative. London: Institute of Child Health. 2002.

UNICEF/UNU/WHO Study team. Multiple micronutrient supplementation during pregnancy (MMSDP): a review of progress in efficacy trials. Bangkok, Thailand organized by the Centre for International Child Health, Institute of Child Health, University College, London and UNICEF/EAPRO. New York:UNICEF 2004.

UNICEF/UNU/WHO/MI. Preventing iron deficiency in women and children. Technical consensus on key issues. Boston: International Nutrition Foundation/Ottawa: Micronutrient Initiative. 1998.

UNICEF/WHO. World Summit for Children- Mid-decade goal: vitamin A deficiency (VAD). UNICEF-WHO Joint Committee on Health Policy. Special Session. Geneva: World Health Organization. JCHPSS/94/2.8 1994a.

UNICEF/WHO. World Summit for Children- Mid-decade goal: iodine deficiency disorders (IDD). UNICEF-WHO Joint Committee on Health Policy. Special Session. Geneva: World Health Organization . JCHPSS/94/2.8 1994b.

UNICEF/WHO. World Summit for Children: Strategic approach to operationalizing selected end-decade goals: Reduction of iron deficiency anaemia. UNICEF-WHO Joint Committee on Health Policy. Special Session. Geneva: World Health Organization. JCHP30/95/4.5. 1995.

UNICEF/WHO Global Meeting on the prevention and control of iron deficiency in children: programmatic guidance (Darnton-Hill I, meeting convener). UNICEF Eastern & Southern Africa Regional Office, Nairobi. July 2006. Internal report- external guidance note under preparation.

UNICEF/WHO/ICCIDD. Progress towards the elimination of iodine deficiency disorders. WHO/NHD/99.4. Geneva: World Health Organization. 1999.

UNICEF/WHO/UNU. Composition of a multi-micronutrient supplement to be used in pilot programmes among pregnant women in developing countries. New York: UNICEF. 1999.

Untoro J, Mangasaryan N, de Benoist B, Darnton-Hill I. Reaching optimal iodine nutrition in pregnant and lactating women and young children: programmatic recommendations. Publ Health Nutr. 2007;10:S1-S3.

UNU/UNICEF/WHO/MI. Preventing iron deficiency in women and children. Technical consensus on key issues and resources for programme advocacy, planning, and implementation. Ottawa: Micronutrient Initiative. 1999.

USAID (Leach M, Kalegaonkar A, Brown LD). PVO perceptions of their cooperation with NGOs. Washington, DC:The Office of Private and Voluntary Cooperation, United States Agency for International Development. 1998.

van der Haar F. The challenge of the global elimination of iodine deficiency disorders. Euro J Clin Nutr. 1997;51:53-8.

Van Stuijvenberg ME, Kvalsvig JD, Faber M, Vorster N, Benade AJS. The hidden hunger: addressing micronutrient deficiencies in school children. Medical Research Council of South Africa: policy briefs. No. 4. 1997.

Veneman AM. The critical role of nutrition for reaching the Millennium Development Goals and success of the Millennium Development project. Background paper delivered by the Executive Director of UNICEF on the occasion of an ECOSOC sponsored event highlighting ‘Maintreaming Nutrition into the MDGs’. New York:UN. 2005.

Victora CG, Wagstaff A, Schellenberg JA, Gwatkin D, Claeson M, Habicht J-P. Applying an equity lens to child health and mortality: more of the same is not enough. Lancet. 2003;362:233-41.

Victora CG, Habicht J-P, Bryce J. Evidence-based public health: moving beyond randomized trials. Am J Publ Health. 2004;94:400-5.

Vijayaraghavan K, Radhaiah G, Prakasam BS, Sarma KVR, Reddy V. Effect of massive dose vitamin A on morbidity and mortality in Indian children. Lancet. 1990;336:1342-5.

Villamor E, Mbise R, Spiegelman D, Hertzmark E, Fataki M, Peterson KE, Ndosi G, Fawzi WW. Vitamin A supplements ameliorate the adverse effect of HIV1, malaria, and diarrheal infections on child growth. Pediatr. 2001;109(1):e6.

Villamor E, Fawzi W, Msamanga G. Human Immunodeficiency Virus Infection. In: Semba RD, Bloem MW (eds.). Nutrition and Health in Developing Countries. 2nd ed. Totowa, NJ: Humana Press. 2007. In press.

Viteri FE. Supplementation for the control of iron deficiency in populations at risk. Nutr Rev. 1997;55:195-209.

Viteri FE. Prevention of iron deficiency. In: Howson C, Kennedy ET, Horwitz A (eds.). Prevention of micronutrient deficiencies: tools for policy makers and public health workers. Washington, DC:National Academy Press. 1998:45-102pp.

Viteri FE, Gonzalez H. Adverse outcomes of poor micronutrient status in childhood and adolescence. Nutr Rev. 2002;60:S77-S83.

Walker SP, Wachs T, Meeks Gardiner J, Lozoff B, Wasserman GA, Pollitt E, Carter JA, and the International Child Development Steering Group. Child development: risk factors for adverse outcomes in developing countries. Lancet. 2007;369:245-57.

Wang X, Qin X, Demirtas H, Li J, Mao G, Huo Y, Sun N, Liu L, Xu X. Efficacy of folic acid supplementation in stroke prevention: a meta-analysis. Lancet. 2007;369:1876-82.

Webb P. Food as Aid: trends, needs and challenges in the 21st century. Rome: World Food Programme. WFP Occasional Paper No.14. 2003:1-29.

Webb P, Coates J, Weinberger K. Despite discrimination: the success of women farmers in a world of constraints. In: Webb, Weinberger (eds.). Women farmers: enhancing rights, recognition and productivity. Frankfurt, Germany: Lang Verlag. 2001.

Webb P, Nishida C, Darnton-Hill I. Age and gender as factors in the distribution of global micronutrient deficiencies. Nutr Rev. 2007;65:233-45.

Webb P, Nishida C, Darnton-Hill I. Intrahousehold dimensions of vitamin and mineral deficiencies: a review of the evidence. Publ Hlth Nutr. In press.

Welch RM, Meisner CA, Hassan N, Duxbury JM, Rutzke M, Fischer PR, Rahman A, Cimma JP, Kyaw-Myint TO, Kabir AL, Talukdern K, Staab DB, Haque S, Combs GF Jr. Mineral status in relation to rickets in Chakaria, Bangladesh. Abstract, Proc Ann Mtg International Centre for the Control of Diarrhoeal Diseases, Bangladesh. Dhaka:ICDDR,B. 1998.

Werner D, Sanders D with Weston J, Babb S, Rodriguez B. Questioning the solution. The politics of primary health care and child survival with an in-depth critique of oral rehydration therapy. Paolo Alto, CA: Healthwrights. 1997.

West CE, Castenmiller JJ. Quantification of the "SLAMENGHI" factors for carotenoid bioavailability and bioconversion. Inter J Vit Nutr. 1998;68:371-7.

West KP Jr. Extent of vitamin A deficiency among preschool children and women of reproductive age. J Nutr. 2002;132:2857S-66S.

West KP Jr, Chirambo M, Katz J, Sommer A, Malawi Survey Group. Breast-feeding, weaning patterns, and the risk of xerophthalmia in Southern Malawi. Am J Clin Nutr. 1986;44:690-7.

West KP Jr, Pokhrel RP, Katz J, LeClerq S, Khatry S, Shrestha S, Pradhan E, Tielsch J, Panday MR, Sommer A. Efficacy of vitamin A in reducing preschool child mortality in Nepal. Lancet. 1991;338:67-71.

West KP Jr, Katz J, Shrestha SR, LeClerq SC, Khatry SK, Pradhan EK, Adhikari R, Wu LS, Pokhrel RP, Sommer A. Mortality of infants under 6 months of age supplemented with vitamin A: A randomized double-masked trial in Nepal. Am J Clin Nutr. 1995;62:143-8.

West KP Jr, Katz J, Khatry SK, LeClerq SC, Pradhan EK, Shrestha SR, Connor PB, Dali SM, Christian P, Pokhrel RP, Sommer A. Double blind, cluster randomised trial of low dose supplementation with vitamin A or Beta-carotene on mortality related to pregnancy in Nepal. The NNIPS-2 study group. Br Med J. 1999;318:570-5.

West KP Jr, Darnton-Hill I. Vitamin A deficiency. In: Semba RD, Bloem MW (eds.). Nutrition and Health in Developing Countries. Preventive Nutrition Series. Totowa, NJ: Humana Press. 2001;chp11:267-306.

West KP Jr, Darnton-Hill I. Vitamin A deficiency. In: Semba RD, Bloem MW (eds.). Nutrition and Health in Developing Countries. 2nd ed. Totowa, NJ: Humana Press. 2007. In press.

WHO. Prevention and control of Iodine Deficiency in Pregnant and lactating women and children under 2 years old. Technical Meeting on iodine supplementation. WHO/UNICEF. 15-16 November 2005.

WHO Regional Office for the Western Pacific. Position paper- Draft. Manila, Philipines: World Health Organization. 1999.

WHO. International Conference on Nutrition. Report by the Director-General to the 91st Session of the Executive Board. Geneva:World Health Organization. EB91/3. 1993:12pp.

WHO. Nutrition: Highlights of recent activities in the context of the World Declaration and Plan of Action for Nutrition. Geneva: World Health Organization. 1995.

WHO. Indicators for assessing vitamin A deficiency and their application in monitoring and evaluating intervention programmes. WHO/NUT/96.10. Geneva: World Health Organization. 1996a.

WHO. Iodized oil during pregnancy: Safe use of iodized oil to prevent iodine deficiency in pregnant women. WHO/NUT/96.5. Geneva: World Health Organization. 1996b.

WHO. A critical link: Interventions for physical growth and psychological development. A review. Department of Child and Adolescent Health and Development. Geneva: World Health Organization. WHO/CHS/CAH/99.3. 1999a.

WHO. Nutrition for health and development. Progress and prospects on the eve of the 21st century. WHO/NHD/99.9. Geneva:World Health Organization. 1999b.

WHO. Vitamin A Supplements: a guide to their use in the treatment and prevention of vitamin A deficiency and xerophthalmia. 3rd Edition. Consultation at Yverdon-les-Bains, Switzerland.

Nutrition for Health and Development Section. Geneva: World Health Organization. 2000. Unpublished.

WHO. Iron deficiency anaemia. Assessment, prevention, and control, a guide for programme managers. UNICEF/UNU/WHO. Geneva: World Health Organization. WHO/NHD/01.3. 2001a.

WHO. Infant and young child nutrition; global strategy for infant and young child feeding. EB109/12. Internal document for Executive Board 109th session. 2001b.

WHO. The World Health Report 2002: Reducing risks, promoting healthy life. Geneva: World Health Organization. 2002.

WHO. World Health Report 2003: shaping the future. Geneva: World Health Organization. 2003a. www.who.int/whr/2003/cn/ (accessed 17 September 2004).

WHO. Nutrient requirements for people living with HIV/AIDS. Report of a technical consultation. May 2003. Geneva:World Health Organization. 2003b.

WHO. Global prevalence of vitamin A deficiency. Geneva: World Health Organization. 2004a. http://www.sightandlife.org/booksAll/BooksHTML/Book05.html (accessed 21 July 2006).

WHO. Iodine status Worldwide. WHO Global Database on Iodine Deficiency. Report by de Benoist B, Andersson M, Egli I, Takkouche B, Allen H. Geneva: World Health Organization. 2004b.

WHO. Health and the Millennium Development Goals: 2005- Keep the promise. Geneva: World Health Organization. 2005a.

WHO. Priorities for research to take forward the health equity policy agenda. WHO Task Force on Research Priorities for Equity in Health and the WHO Equity Team. Bull Wld Hlth Org. 2005b;83:948-53.

WHO. The World Health Report 2005: Make every mother and child count. Geneva: World Health Organization. 2005c.

WHO. Database on anaemia. Vitamin and Mineral Nutrition Information System (VMNIS). 2007. http://www.who.int/vmnis/anaemia/data/database/countries/en/index.html (accessed 13 July 2007).

WHO. Reaching optimal iodine nutrition in pregnant and lactating women and young children. Report of an Expert Consultation. Geneva: World Health Organization. In press.

WHO/CDC. Assessing the iron status of populations. Report of a Joint World Health Organization /Centers for Disease Control and Prevention. Technical Consultation on the assessment of iron status at the population level. Geneva: WHO. 2004.

WHO/CHD. Immunization-linked Vitamin A Supplementation Group. Randomized trial to assess benefits and safety of vitamin A supplementation linked to immunization in early infancy. Lancet. 1998;352:1257-63.

WHO/FAO. Human vitamin and mineral requirements. Report of a Joint FAO/WHO Expert Consultation. Rome:Food & Agriculture Organization of the United Nations. 2002. ftp://ftp.fao.org/es/esn/nutrition/Vitrni/vitrni.html (accessed 25 December 2004).

WHO/FAO. Diet, nutrition and the prevention of chronic diseases. Report of a Joint WHO/FAO Expert Consultation. WHO Techn Rep Ser No.916. Geneva: World Health Organization. 2003.

WHO/FAO (Allen L, de Benoist B, Dary O, Hurrell R (eds.). Guidelines on food fortification with micronutrients for the control of micronutrient malnutrition. Geneva: World Health Organization. 2006.

WHO/MI. Safe vitamin A dosage during pregnancy and lactation; recommendations and report of a consultation. WHO/NUT/98.4. Geneva: World Health Organization. 1998.

WHO/UNICEF. Global prevalence of vitamin A deficiency. MDIS Working paper #2. Geneva:World Health Organization. WHO/NUT/95.3. 1995.

WHO/UNICEF. Focusing on anaemia: Towards an integrated approach for effective anaemia control- WHO/UNICEF Joint Statement. Geneva: World Health Organization. 2004a.

WHO/UNICEF. Clinical management of acute diarrhea- WHO/UNICEF Joint Statement. New York: UNICEF. 2004b.

WHO/UNICEF/ IVACG. Global prevalence of vitamin A deficiency. MDIS Working paper No. 2. WHO/NUT/95.3. Geneva: World Health Organization. 1995.

WHO/UNICEF/IVACG Taskforce. Vitamin A Supplements: a guide to their use in the treatment and prevention of vitamin A deficiency and xerophthalmia. 2rd ed. Geneva: World Helath Organization 1997.

WHO/UNICEF/ICCIDD. Global prevalence of iodine deficiency disorders. Micronutrient Deficiencies Information System (MDIS) Working Paper No.1. Geneva: World Health Organization. 1993.

WHO/UNICEF/ICCIDD. Indicators for assessing iodine deficiency disorders and their control through salt iodization. WHO/NUT/94.6. Geneva: World Health Organization. 1994.

WHO/UNICEF/ICCIDD. Progress towards the elimination of iodine deficiency disorders. Geneva: World Health Organization. 1999. Unpublished document WHO/NHD/99.4.

WHO/UNICEF/ICCIDD. Assessment of iodine deficiency disorders and monitoring their elimination. 2nd ed. WHO/NHD/01.1. Geneva: World Health Organization. 2001.

WHO/UNICEF/UNU. Iron deficiency anaemia: assessment, prevention, and control. A guide for programme managers. WHO/NHD/01.3. Geneva: World Health Organization. 2001.

WHO/WFP/UNICEF. Joint statement on preventing and controlling micronutrient deficiencies in populations affected by an emergency. Geneva: World Health Organization. 2005.

Wibulpolprasert S, Tangcharoensathien V, Kanchanachitra C. Are cost-effective interventions enough to achieve the Millennium Development Goals? Br Med J. 2005;331:1093-4.

Wolf G. A history of vitamin A and retinoids. FASEB J. 1996;10:1102-7.

World Bank. Global Alliance for Improved Nutrition. Mission statement and basic information. Available from: www.worldbank.org (accessed 15 June 2002).

World Bank. Investing in Health: World Development Report 1993. New York: Oxford University Press. 1993.

World Bank. Enriching Lives: Overcoming vitamin and mineral malnutrition in Developing Countries. Development in Practice Series. (prepared by McGuire J, Galloway R). Washington, DC: World Bank. 1994.

World Bank. Attacking Poverty: World Development Report 2001.Oxford: Oxford University Press. 2001.

World Bank. The Millennium Development Goals for health: rising to the challenge. Washington,DC: World Bank. 2004a.

World Bank. Global monitoring report 2004: Policies and actions for achieving the Millennium Development Goals and related outcomes. Washington,DC: World Bank. 2004b:250pp.

World Bank. Repositioning nutrition as central to development. A strategy for large-scale action-Directions in Development. Washington,DC: World Bank. 2006a.

World Bank. Equity and development: World Development Report 2006. Washington,DC: World Bank. 2006b.

WTO. TRIPS (Trade-related aspects of intellectual property rights). www.wto.org/english/tratop_e/trips_e/trip_e.htm (accessed 27 May 2007).

Yach D, Kellogg M, Voute J. Chronic diseases: an increasing challenge in developing countries. Trans Roy Soc Trop Med Hygiene. 2005;99:321-4.

Yip R. Iron supplementation: country level experiences and lessons learned. J Nutr. 2002;132(Suppl4):859S-61S.

Yip R, Stoltzfus R, Simmons WK. Assessment of the prevalence and the nature of iron deficiency for populations: the utility of comparing haemoglobin distributions. In: Hallberg L, Asp N-G (eds.). Iron Nutrition in Health and Disease. London:John Libbey. 1996:31-8pp.

Zimmerman R. Let them eat Cheez Whiz? The Wall Street Journal. 2002 May 9.

Zimmermann MB, Saad A, Hess S, Torresani T, Chaoki N. Thyroid ultrasound compared with World Health Organization 1960 and 1994 palpation criteria for determination of goitre prevalence in regions of mild and severe iodine deficiency. Euro J Endocrinol. 2000:143:610-14.

Zimmermann MB, Hess SY, Adou P, Toresanni T, Wegmüller R, Hurrell RF. Thyroid size and goiter prevalence after introduction of iodized salt: a 5-year prospective study in schoolchildren in Côte d'Ivoire. Am J Clin Nutr. 2003;77:663-7.

Zimmermann MB, Wegmüller R, Zeder C, Chaouki N, Torresani T. The effects of vitamin A deficiency and vitamin A supplementation on thyroid function in goitrous children J Clin Endrocrinol Metab 2004a;89:5441-7.

Zimmermann MB, Wegmüller R, Zeder C, Chaouki N, Rohner F, Torresani T, Hurrell R. Triple fortification of salt with microencapsulated iodine, iron and vitamin A: a randomized, double-blind trial. XXII IVACG Meeting, Lima, Peru: vitamin A and the common agenda for micronutrients. 2004b:Abstract M62.

Zinc Investigators' Collaborative Group (Bhutta ZA, Black RE, Brown KH, Meeks-Gardner J, Gore S, Hidayat A, Khatun F, Martorell R, Ninh NX, Penny ME, Rosado JL, Roy SK, Ruel M, Sazawal S, Shankar A). Prevention of diarrhea and pneumonia by zinc supplementation in children in developing countries: Pooled analysis of randomized controlled trials. J Pediatr. 1999;135: 689-97.

Zlotkin S, Arthur P, Antwi KY, Yeung G. Randomized controlled trial of microencapsulated ferrous fumarate 'sprinkles' and ferrous sulfate drops, for the treatment and prevention of anemia in Ghanaian infants. In: XXth IVACG Report '25 Years of progress in controlling Vitamin A

deficiency: looking to the future'. Washington, DC:IVACG/USAID/ILSI Research Foundation. Abstracts. 2001;F47:30.

Zlotkin S, Tondeur, MC. Successful approaches- Sprinkles. In: Kraemer K , Zimmerman MB (eds.). Nutritional Anaemia. Basel: Sight & Life Press. 2007;chp17:269-284.